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AIRWAY MANAGEMENT IN PATIENTS WITH POLIOMYELITIS

ELECTIVE TRACHEOTOMY AND TRACHEAL INTUBATION

Hamilton S. Davis, M.D.
and
Harold F. Bishop, M.D., Valhalla, N. Y.

There is controversy, at present, concerning the place of early (so-called elective or prophylactic) tracheotomy in the supportive treatment of acute anterior poliomyelitis with severe respiratory involvement. Those who oppose its use, exemplified in the literature by Stimson [1] and Sweet,[2] claim comparable results with conservative treatment, with tracheotomy used as a last resort. Galloway,[3] Weiland,[4] Brown and associates,[5] and West and Bower,[6] on the other hand, favor it as the most effective means of combating obstruction of the airway by secretions and vocal cord palsy. It would appear the trend in recent years has been toward the latter approach, particularly in the larger poliomyelitis centers.

It seems apparent that two phases of the problem exist. Initially, the patient must be protected from early asphyxial death resulting from high respiratory tract obstruction, pulmonary edema, and hypoventilation. Later, lower respiratory tract obstruction with its subsequent atelectasis and pneumonitis, which is the frequent sequel to hypoventilation and inability to cough, must be combated. Practically all who die after surviving the initial phase do so because of pulmonary complications, in spite of antibiotic therapy.

It would seem, therefore, the treatment of choice would be that which coped most effectively with both phases. Unfortunately, reports to date have dealt predominantly with the primary disease process, describing only in a general way the morbidity and mortality arising from pulmonary complications. Such data must be reported carefully, for only by its accumulation can some answer be reached regarding effective therapy. There are so many variables that a controlled study is almost impossible; the only hope seems to lie in the accumulation of enough clinical and pathological data to permit a relatively objective conclusion.

Because of several factors, there was a swing from conservative management, at our hospital, to the use of the early tracheotomy. First, the conservative method had left much to be desired, there having been patients thus treated who, in retrospect, might have fared better with early tracheotomy. Second, we were favorably impressed with the results of tracheotomies in comatose patients, whose respiratory problems simulate those of patients with poliomyelitis. Third, we felt that the writers stressing this method presented rather convincing logic. Also, the virulence of the disease in 1949, with its high incidence of severe bulbar forms, influenced our decisions. To cope with this entire problem, a "poliomyelitis team," of which the anesthesiologist was a member, was formed. The resuscitative features presented in handling these patients, many of whom were children, led to the development of a technique that has not, to our knowledge, been reported elsewhere in the English literature. Certain aspects of this technique are original; however, it must be pointed out that many features in the over-all plan have been borrowed from the works of Galloway,[3] Brown and co-workers,[5] and Leigh and Belton.[7] The purpose of this discussion, then, is twofold: to present a treatment plan based on the use of early tracheotomies in patients with poliomyelitis and to give the results, with emphasis being placed on morbidity due to respiratory involvement as well as mortality.

From the Department of Anesthesiology, Grasslands Hospital.
Read in part before the Annual Meeting of the American Society of Anesthesiologists, Inc., New York, Dec. 10, 1949.

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2. Sweet, L. K.: Acute Anterior Poliomyelitis: Diagnosis, Differential Diagnosis and Treatment of Bulbar Paralysis and Respiratory Failure, M. Ann. District of Columbia **14**: 501-504 (Nov.) 1945.
3. Galloway, T. C.: Management of Respiratory Complications of Poliomyelitis, Arch. Otolaryng. **46**: 125-136 (Aug.) 1947.
4. Weiland, A. H.; Burbacher, C. R., and Keiser, R. P.: Management of Bulbar Poliomyelitis, South. M. J. **40**: 157-161 (Feb.) 1947.
5. Brown, J. R.; Baker, A. B., and McQuarrie, I.: Bulbar Form of Poliomyelitis: Therapeutic Measures Based on Pathologic and Physiologic Findings, J. A. M. A. **135**: 425-428 (Oct. 18) 1947.
6. West, H. E., and Bower, A. G.: Treatment of Poliomyelitis Involving the Respiratory System, Am. J. M. Sc. **217**: 252-255 (March) 1949.
7. Leigh, M. D., and Belton, M. K.: Pediatric Anesthesia, New York, The Macmillan Company, 1948, pp. 142-143.

DEFINITIONS

It is appropriate, at this time, to list certain definitions as we have employed them in our study.

Disease Classification.—Three types of acute poliomyelitis have been recognized in our series of cases: spinal, bulbar, and bulbospinal. "Encephalitic" manifestations have been deliberately excluded because of their questionable clinical differentiation, in most instances, from hypoxic reactions. That there is actual invasion of the cerebral hemispheres by the disease process in certain cases has been demonstrated pathologically by Brown and co-workers [5] and Bodian [8] and in our own material. However, whether such minimal involvement as has been described in these regions is of clinical significance is debatable. There were no so-called pure encephalitic forms in this series.

1. Spinal Type: This type indicated involvement of spinal nerves only, as determined clinically. All patients coming to autopsy revealed involvement of higher centers; the diagnosis of spinal type was, of necessity, a clinical diagnosis only.

2. Bulbar Type: This type indicated involvement of medullary centers and cranial nerves only, as determined clinically or pathologically.

3. Bulbospinal Type: This type indicated involvement of medullary centers, cranial nerves, and spinal nerves, in combinations, as determined clinically or pathologically. This type predominated.

Pulmonary Complication.—The diagnosis of pulmonary complication was made whenever clinical, roentgenographic, or pathological findings indicated significant involvement of the lung parenchyma. Included also was severe tracheobronchial disease; not included were minor degrees of tracheobronchitis associated with the expected trauma of the tracheotomy tube and the frequent tracheal suctioning. For the sake of this study, borderline conditions were considered as pulmonary complications; the figures presented are, therefore, maximum.

TREATMENT

Our treatment schedule may be divided into three periods for the sake of description: the evaluation period, the anesthesia-operative period, and the postoperative period.

Evaluation Period.—When a patient has respiratory dysfunction, whether it be spinal or bulbar in origin, he is observed closely by the poliomyelitis team. This team is composed of appropriate representatives of the medical or pediatric, neurology, otolaryngology, and anesthesiology services. In the evaluation period conservative measures of positioning, suctioning, oxygenation, hydration, administration of antibiotics, and proper nutrition are practiced by special nurses. During this time, the patient is examined frequently for progressing disease; it is emphasized that respiratory failure represents a concrete danger, whereas the "fatigue" secondary to such examinations is largely hypothetical. If the team decides the patient is becoming worse with conservative therapy, a tracheotomy is performed in the operating room. After this, he is placed in the respirator, if indicated. Indications for tracheotomy and use of the respirator are similar to those first outlined in 1943 by Galloway [9] and emphasized by others since. This is, by choice, an elective procedure. The "last-ditch" or "stab" tracheotomy is mentioned only to condemn it, or, at best, to relegate it to emergency conditions in the field in which proper equipment and personnel may not be available.

Anesthesia-Operative Period.—When the team decides that tracheotomy is advisable, a belladonna drug is given to facilitate the subsequent intubation of the trachea. Sedation is not necessary in these cases and may be dangerous. The anesthesiologist decides whether the patient is in immediate need of oxygen only, of a patent airway, or both. If he shows minimal obstruction and is getting along reasonably well with nasal administration of oxygen, he is transported to the operating room with oxygen.

With airway obstruction in a conscious patient, endotracheal intubation is accomplished on the ward with topical anesthesia, 10% cocaine being carefully applied to the pyriform fossa bilaterally through pledgets on curved laryngeal forceps. Only minimal anesthesia is necessary in most cases, because of the diminished gag reflex. It is imperative that a good source of suction be available during this time, because of the hypersecretion present. Tracheal intubation under direct laryngoscopy is preferable to the blind nasal method, as the latter frequently necessitates several attempts, thus increasing the possibilities of trauma and hypoxia. The curved MacIntosh laryngoscope blade has proved the most effective for these intubations. Magill endotracheal forceps for directing the catheter should always be at hand.

In those semiconscious or unconscious patients who need rapid resuscitation, it is neither necessary nor advisable to waste time with cocainization; intubation is carried out as quickly as possible and is not infrequently lifesaving. The nasotracheal route, with direct laryngoscopy, is useful on the ward, as the tube is less likely to become dislodged while the patient is en route to the operating room than if orotracheal intubation is used. The airway thus assured, there is almost always spontaneous improvement in the condition of the patient, often with a return to consciousness. The endotracheal tube is well tolerated without further anesthesia, although "bucking" is always present with suctioning attempts down as deep as the carina. If necessary, respirations are compensated by manual pressure on the breathing bag of a closed to and fro carbon dioxide absorption system connected to a source of oxygen. The danger of asphyxia now past, the patient is taken safely to the operating room on a stretcher equipped with oxygen and capable of being placed in the head-down position, the latter facilitating removal of secretions and vomitus.

Tracheotomies have long been done with local anesthesia with or without a bronchoscope in the trachea. It is felt this is not the safest procedure in patients who, by the nature of their disease, have reduced ventilatory capacity. It is our impression that much of the criticism leveled at the use of tracheotomies in these cases stems from the use of this method. Although local anesthesia has undeniable advantages in the proper situation, it can

8. Bodian, D.: Histopathologic Basis of Clinical Findings in Poliomyelitis, Am. J. Med. **6**: 563-578 (May) 1949.

9. Galloway, T. C.: Tracheotomy in Bulbar Poliomyelitis, J. A. M. A. **123**: 1096-1097 (Dec. 25) 1943.

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be completely unsatisfactory in terrified, uncooperative patients, especially children. Fear and struggling lead to increased oxygen requirement, trauma with the bronchoscope, and hurried bloody tracheotomies, during which time the circulating epinephrine of the surgeon, as well as the patient, probably reaches considerable levels. For this reason, general anesthesia with the gaseous agents has been adopted in our clinic and has proved satisfactory. Cyclopropane, ethylene, and, on occasion, nitrous oxide are used. These can be applied in such combinations as to provide rapid quiet induction, light maintenance, high oxygen tensions, and almost immediate recovery. They have relatively transient effects on the various organs and are not respiratory tract irritants in the concentrations used.[10] The use of cyclopropane might be objectionable on theoretical grounds in those patients with myocarditis, which is frequently a finding associated with this disease in its severer forms. However, in clinical practice, to date, no ill-effects have been noted, and this gas has been the primary agent in every case. Of interest is the ease of induction and maintenance of anesthesia with minimal amounts of agent in this group of anxious, febrile young patients without premedication other than the use of belladonna drugs. This paradox apparently reflects the altered oxidation processes in the central nervous system in patients with poliomyelitis; it warns against overdosage during the anesthetic management.

In the induction of anesthesia, the breathing bag is filled with oxygen, and then a flow of equal volumes of oxygen and cyclopropane is introduced, usually 500 cc. of each in the adult and smaller volumes in small children, until consciousness is lost. An endotracheal tube is, of course, already in place, having been inserted either on the ward or in the operating room by means of the technique previously described. After induction, a constant flow rate of 5% to 20% cyclopropane with oxygen is maintained, depending on the patient's requirements. A to and fro absorption system has proved to be most adaptable with regard to reduction of dead space and breathing resistance to a minimum, portability features, and ease of sterilization; no doubt a circle absorption method could be adapted satisfactorily. In the subsequent sterilization of the equipment, it might be mentioned here, a dilute formaldehyde solution in alcohol is used for rubber and plastic parts, metal parts being autoclaved.

The surgeon now enters the trachea through a surgical field in which the aim is careful hemostasis. The site of the tracheotomy is, of course, the surgeon's choice. The highest safe tracheotomy, usually through the third tracheal ring, has proved best for subsequent respirator care. At this time the tip of the endotracheal tube is withdrawn just proximal to the tracheal window created. Anesthesia is continued with a high gas flow to compensate for the opening. A mixture of 45% ethylene, 5% cyclopropane, and 50% oxygen is about right, with a total flow of 2 to 5 liters per minute. The trachea is aspirated by the surgeon and the appropriate size of tracheotomy tube inserted. A thin-walled endotracheal catheter, which will fit the tube snugly, is chosen from a previously sterilized set of graduated sizes. The distal end is fitted into the tracheotomy tube by the surgeon; the proximal end is passed through the drape opening to the anesthetist, who attaches it to the canister by means of the usual connectors. Care is exercised to keep dead space minimal. Closed anesthesia is then resumed with a small flow of gasses. One must be careful, at the above stage, not to exert undue positive pressure in the system; mediastinal emphysema could result. It did not occur in this series. The wound is closed in layers and dressed and the flow of anesthetic agent terminated. The patient is awake in a few minutes unless other factors intervene. If he is breathing adequately, he is returned to the ward with oxygen being given through a small catheter in the tracheotomy tube opening. If the respirator is necessary, manually assisted respirations are continued by means of the still attached canister and bag until the patient is placed in the machine.

Postoperative Period.—Survival now depends on two factors: progression of the disease and respiratory complications. At present, we have no control over the former; treatment is directed toward preventing the latter. It has been found that the patients with bulbar disease whose main problem is one of obstructed airway and aspiration, get along well once a free airway is established by means of their tracheotomy. It is felt that with this prophylactic tracheotomy the patient has a greater chance to escape the dangers of aspiration and is offered the best possibilities of vigorous treatment if they do occur. One patient (J. W., table 3) was unquestionably saved from an asphyxial death on two separate occasions during his convalescence, when he vomited and aspirated large quantities of tube feedings. Only prompt evacuation of his tracheobronchial tree by means of a catheter through his tracheotomy and the head-down position saved his life. Equally gratifying was the lack of detectable respiratory complications following these two episodes.

When the respirator enters the picture, the outlook is graver. We have used both cuirass and cylinder type respirators. The former has proved an adjunct to, but not a substitute for, the latter. Its nursing advantages are obvious, but, in our hands, the respiratory exchange has not approached that of the cylinder type. The use of a curved metal brace to push the rubber collar into the machine, leaving the tracheotomy outside and easily accessible, has greatly facilitated care of the airway when the cylinder respirator is used. Such braces are available commercially. In addition, as mentioned previously, a rather high tracheotomy is preferable, so that it is as far outside the collar as possible. Too high tracheotomy is to be avoided, however, because of the danger of subsequent laryngeal stenosis, a formidable complication.

To reduce pulmonary complications in the respirator, it is axiomatic that patent tracheobronchial passages and near normal mucous membranes be maintained. That by-passing the upper respiratory tract disrupts certain important physiological processes cannot be denied. The aim is to lessen this insult so that the advantages outweigh the disadvantages. To this end, the nurses are instructed individually in the essentials of proper care for these patients. This includes the correct method of suctioning the trachea, mouth, and nose; the systematic ro-

10. Adriani, J.: The Pharmacology of Anesthetic Drugs: A Syllabus for Students and Clinicians, ed. 2, Springfield, Ill., Charles C Thomas, Publisher, 1942, pp. 17-24.

tation of the patient through the lateral, Fowler, and Trendelenburg positions; the desired oxygen flow rates and humidification; the appropriate respirator pressures and rates; and the care of the patient's skin. The symptoms and signs of hypoxia are reviewed for them. In short, painstaking attention to detail is taught.

A few points on care of the tracheotomy might be mentioned. The otolaryngologist of the team uses a rather long incision, 3 to 4 cm. in adults, closes the wound in layers, and, therefore, does not remove the outer tube initially in less than 72 hours, thus insuring adequate canalization. Subsequently, it is removed, cleaned, and replaced daily. The inner tube is removed and cleaned at least every three hours. Suctioning through the tracheotomy is done by means of low pressures through sterile, terminal orifice, soft rubber catheters. This is carried out rapidly to avoid marked reductions in arterial blood oxygen saturation.

Bronchoscopy is easily performed through the tracheal stoma, even with the patient in the cylinder respirator; the cuirass respirator facilitates this procedure and has proved valuable in this respect. Bronchoscopic aspiration is used without hesitation and, if necessary, repeatedly, when atelectasis occurs. Pounding the chest at intervals is helpful in dislodging thick secretions. Adequate hydration is an absolute necessity to keep secretions thin; to insure this, intravenous polyethylene catheterizations by cutdown have been used almost routinely during the first 48 hours in the respirator, after which tube feeding is attempted. The use of belladonna-like drugs, at this point, is contraindicated. It may be helpful to administer potassium iodide to liquefy secretions.

Curare type compounds are occasionally of great value in the treatment of patients who exhibit such intercostal muscle spasm as to reduce tidal exchange significantly. Intravenous administration of small repeated doses, of the order of 3 to 6 mg. (1 to 2 cc.) of *d*-tubocurarine hydrochloride, or similar drugs in comparable doses, usually suffices; larger doses may be given without fear of adverse respiratory effects, if necessary, in a tracheotomized patient in the respirator. However, histamine-like reactions on the vascular system may follow the administration of large doses of *d*-tubocurarine, so that caution is advisable. Sedation may be used, when it is felt necessary, at this stage in the management of the patient. It was seldom needed in our series. It is contraindicated in the early stages of the illness as mentioned previously.

Weaning from the respirator is a complex procedure in some patients, requiring the utmost ingenuity on the part of the physician. The psychic factors involved are by far the most important. The patient rapidly acquires a dependency on the machine, which increases as time passes. In general, it has been the policy to get them out, for gradually increasing time intervals, at the earliest possible moment. This may mean within a few hours after entry in some instances. Tracheotomies are closed when the patient no longer depends on the machine or, in cases of bulbar disease, when protective pharyngeal and laryngeal reflexes have returned.

Antibiotics are used freely. It is a well-known fact, however, that their use will not prevent infection in portions of the lung that are not aerating properly and from which secretions cannot drain because of obstruction in the bronchial tree.

Paralyzed excretory functions are supported by the use of bladder catheterization and enemas until normal function is restored. The value of the use of stimulating drugs for these functions is questionable.

RESULTS

There were 229 cases of diagnosed acute poliomyelitis in our hospital during the seasons of 1948 and 1949 (83 cases in 1948 and 146 in 1949). The ratio of males to females over the two-year period was 53% to 47% and that of children to adults 60% to 40%. The latter figures are based on adulthood placed at 12 years for females and 16 years for males. All the patients were white.

In 1948, there were 18 (22%) patients with bulbur disease, the majority of these also having associated spinal paralysis. In addition, one patient had severe intercostal paralysis without bulbar signs. There were, therefore, 19 (23%) seriously ill patients. Six (7%), including one child and five adults, were placed in the respirator (table 1). All six had tracheotomies, two before being placed in the machine and four afterward, because of obvious respiratory problems. No other tracheotomies were performed in 1948.

In the 1948 series, two patients (2.5%) died. Both had bulbospinal disease with pulmonary complications proved at autopsy; both had been placed in the respirator without preceding tracheotomies. Of the four who survived, two had clinical evidence of pulmonary complications at some time during their illness. Therefore, 66% of respirator patients had respiratory complications. It is of interest that the two patients who were forced to remain in the machine over two weeks both survived and that neither showed evidence of pulmonary complications at any time.

TABLE 1.—*Child and Adult Tracheotomy-Respirator Cases—1948*

Patient	Age (Yr.), Sex	Type of Disease	Treatment*		Time in Respirator		Pulmonary Complications		Result	
			Tracheotomy	Respirator	Less Than Two Weeks	More Than Two Weeks	Yes	No	Lived	Died*
J. T.	20, F	Bulbospinal	HD 4	HD 1 †	..	x	x	..	x	.....
L. F.	4, M	Bulbar	HD 0	HD 1	x	..	..	x	x	.....
D. M.	16, M	Spinal	HD 3	HD 3 †	x	..	..	x	x	.....
B. M.	24, F	Bulbospinal	HD 2	HD 2	..	x	x	.	x	.....
K. O.	14, F	Bulbospinal	HD 2	HD 0 †	x	..	x	..	..	HD 2 ‡
D. H.	34, F	Bulbospinal	HD 1	HD 1 †	x	..	x	..	..	HD 11 ‡
Total	.....	.....	6	6	4	2	4	2	4	2

* HD = hospital day; HD 0 = day of admission. † Respirator treatment preceded tracheotomy. ‡ Complete autopsy.

In the outbreak in 1949 there were far more virulent characteristics, in addition to almost double the total number of cases. Thirty-nine (27%) had bulbar involvement, the majority associated with spinal paralysis. Five others had severe intercostal paralysis without bulbar signs, which brings the total to 44 seriously ill, or 30%. Fifteen (10%), including six children and nine adults, were placed in the respirator. (tables 2 and 3). All patients who were placed in respirator had tracheotomies, 12 before being placed in the machine and the remaining 3 later. There were, in addition, three tracheotomies performed on patients who did not require the respirator. The total number of patients subjected to tracheotomy in 1949 was 18.

Two facts are apparent in these 229 cases. Of the 24 most critically ill, 18 (75%) were females and 16 (66%) were adults. This in spite of the fact that males and children predominated in the series as a whole. As might be expected with the above ratio of seriously ill, of the 13 mortalities (5.7) over the two years, the majority were females and adults; 10 were females and 8 were adults.

Eleven of the 13 patients who died had complete autopsies. Two of these had evidence of major atelectasis; six others showed, in varying degrees, minute atelectatic foci in the peripheral lung fields, lobular pneumonia, and pulmonary congestion and edema that was frequently hemorrhagic. It was believed that, with one or two exceptions, these deaths were due to central nervous system failure, not pulmonary disease. Many were sudden and unexpected in patients who seemed to be getting along not too badly. The commonest sites of nervous system involvement were the spinal cord anterior horn cells, the floor and roof of the fourth ventricle, and the bulbar reticular formation. Generalized hemorrhagic manifestations were present in some of the patients; however, these may have been agonal. Nine of the 11 showed myocarditis of varying degrees.

TABLE 2.—*Child Tracheotomy-Respirator Cases—1949*

Patient	Age (Yr.), Sex	Type of Disease	Treatment*		Time in Respirator		Pulmonary Complications		Result	
			Tracheotomy	Respirator	Less Than Two Weeks	More Than Two Weeks	Yes	No	Lived	Died*
W. B.	8, F	Bulbospinal	HD 0	HD 0	..	x	x	..	..	HD 17 ‡
J. P.	7, F	Bulbospinal	HD 1	.....	..	..	x	..	x	.....
G. V.* B.	9, F	Bulbospinal	HD 0	HD 0	x	..	x	..	..	HD 3 ‡
F. D.	11, F	Spinal	HD 1	HD 0 †	x	..	x	..	x	.....
P. R.	10, F	Bulbar	HD 0	HD 0	x	..	..	x	x	.....
J. S.	4, F	Bulbospinal	HD 1	HD 1	x	..	x	..	..	HD 4
B. N.	5, M	Bulbospinal	HD 1	HD 1	x	..	x	..	..	HD 1 ‡
Total	.....	.....	7	6	5	1	6	1	3	4

* HD = hospital day; HD 0 = day of admission. † Respirator treatment preceded tracheotomy. ‡ Complete autopsy.

TABLE 3.—*Adult Tracheotomy-Respirator Cases—1949*

Patient	Age (Yr.), Sex	Type of Disease	Treatment*		Time in Respirator		Pulmonary Complications		Result	
			Tracheotomy	Respirator	Less Than Two Weeks	More Than Two Weeks	Yes	No	Lived	Died*
M. M.	32, F	Bulbospinal	HD 4	HD 4	x	..	..	x	x	.....
A. C.	27, F	Bulbospinal	HD 1	HD 1	x	..	..	x	..	HD 2 ‡
H. J.	29, F	Bulbospinal	HD 2	HD 2 †	..	x	..	x	x	.....
M. F.	30, F	Bulbospinal	HD 2	HD 2	x	..	x	..	..	HD 4 ‡
R. W.	18, F	Bulbospinal	HD 0	HD 1	..	x	x	..	x	.....
J. W.	33, M	Bulbar	HD 0	.....	..	..	..	x	x	.....
K. R.	24, F	Bulbospinal	HD 3	HD 3	..	x	x	..	..	HD 41 ‡
D. C.	24, M	Bulbospinal	HD 2	HD 2 †	x	..	x	..	..	HD 7 ‡
J. E.	15, F	Bulbospinal	HD 1	HD 1	..	x	..	x	x	.....
J. C.	22, M	Bulbar	HD 0	.....	..	..	? §	?	..	HD 0
J. D.	24, F	Bulbospinal	HD 0	HD 0	x	..	..	x	x	.....
Total	.....	.....	11	9	5	4	4	6	6	5

* HD = hospital day; HD 0 = day of admission. † Respirator treatment preceded tracheotomy. ‡ Complete autopsy. § Patient died a few hours after admission; no autopsy.

In the 1949 series, 11 patients (7.5%) died; all had bulbar involvement, the majority with associated spinal paralysis. Eight of the 15 placed in respirators died; seven of these deaths were associated with pulmonary complications. Of the seven respirator patients who survived, three had similar complications. From these figures it is evident that 10 (66%) of the 15 respirator patients had complicating respiratory infections. Of the 18 patients subjected to tracheotomy, 9 (50%) died; in 10 (55%) the disease was complicated by respiratory infections. There were five patients in whom the machine was required for more than two weeks; two died and three lived. Both patients who died had pulmonary complications at autopsy; of the three survivors, two had no evidence of respiratory infection at any time.

SUMMARY

Two hundred twenty-nine patients with acute anterior poliomyelitis were admitted to a county hospital during the seasons of 1948 and 1949. The outbreak of 1949 in

Westchester County, New York, was, as in other parts of the country, extremely virulent. There was a predominance of adults and females in the critically ill group.

The management of the severe respiratory dysfunction presented by 24 of these patients is discussed. The role of a "poliomyelitis team" composed of representatives of the interested services is suggested. The essentials involved are endotracheal intubation, resuscitation, and early tracheotomy, with the use of the respirator when indicated. The part played by the anesthesiologist in this regimen is outlined.

The importance and incidence of pulmonary infection as a complicating factor in these cases is stressed. This is particularly true of the patients placed in the respirator, 66% of these having such complications. A plea is made for detailed reports from other larger clinics on this phase of the disease, in order that the role of early tracheotomy in preventing and treating these complications might be evaluated.

ULTRAVIOLET IRRADIATION OF BLOOD IN MAN

STUDIES OF SIXTY-EIGHT PATIENTS

Steven O. Schwartz, M.D., Sherman R. Kaplan, M.D., James Stengle, M.D., Fern L. Stevenson, M.D.
and
Mary Vincenti, Chicago

Comparatively recent interest in ultraviolet rays as a means of sterilization stimulated us to investigate the value of this therapeutic method. The fountainhead of interest in the beneficial effects of ultraviolet irradiation of blood is E. K. Knott,[1] who, working from the premise that ultraviolet rays have bactericidal properties, devised an ingenious apparatus for the purpose of irradiating whole blood. He recognized early "that the source of the ultraviolet energy was inconstant and varied widely" and would "produce variable results and often a failure to obtain measurable results." Because of this, "A source of ultraviolet of known intensity was sought that could be easily controlled so that a uniform dosage could be achieved and duplicated at will."

EARLY EXPERIMENTATION

Animals.—When animal experiments were first begun, the animals died of overirradiation. Eventually the premise was evolved, from experiments on bacteremic animals, "that it was neither necessary to expose the blood sufficiently to kill the bacteria directly . . . nor to expose all of the blood to achieve a desired effect upon the entire blood stream." The total amount of blood to be irradiated was determined to be from one-sixteenth to one-twentieth of the estimated blood volume, or approximately 1.5 cc. per pound (3 cc. per kilogram) of body weight. Because direct bactericidal action could not account for the good results, ". . . a corrected or extended hypothesis was established." It was suggested that impingement of small, carefully regulated doses of selected ultraviolet rays directly on the blood stream in some way (1) increased the bactericidal properties; (2) exerted some influence on the vital resistance factors of the host, enabling it to overcome the infection and to progress to complete recovery; and (3) exerted some influence on the toxic conditions produced by the disease, either by direct action on the toxins or by indirect action through the host's rallied defense mechanisms.

Human Treatment.—The first treatment of a human being took place in 1928, when the blood of a dying woman who had had a septic abortion, complicated by hemolytic streptococcic bacteremia, was irradiated. The patient responded favorably and recovered uneventfully. During this period Knott wrote:

> . . . experiments were conducted to try to determine what particular component of the blood was most profoundly affected by ultraviolet irradiation and in what manner. This work had to be curtailed without definite results being obtained because of the difficulty of following the *chain chemical reactions* set up and the lack of equipment and money to pursue them to conclusion.

It seems that fundamental investigations into the effects of ultraviolet blood irradiation were abandoned, and ". . . clinical observations seemed . . . to be the most important procedure to follow next until sufficient knowledge could be accumulated from the use of the procedure upon which to base problems of basic research."

Favorable Reports.—In 1934 Hancock and Knott [2] published the first of a series of articles dealing with clinical results. In the intervening 17 years, since the procedure was turned over to clinicians and has come into more or less general use, sporadic articles have appeared purporting to show the beneficial effects of reinfused irradiated human blood. The most recent publications are almost exclusively from the United States. These articles laud the effects of ultraviolet irradiation in thrombophlebitis,[3] staphylococcemias,[4] botulism,[5] poliomyelitis,[6] nonhealing wounds,[7] acute pyogenic infections,[8] peritonitis,[9] acute infections,[10] and asthma.[11] Acute virus and virus-like infections [12] have been said to re-

Dr. Stevenson was a Hematology Research Foundation Fellow.
From the Hematology Laboratory and the Hektoen Institute for Medical Research of the Cook County Hospital.
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1. All quotations in this communication are from Knott, E. K.: Development of Ultraviolet Blood Irradiation, Am. J. Surg. **76**: 165 (Aug.) 1948.
2. Hancock, V. K., and Knott, E. K.: Irradiated Blood Transfusion in the Treatment of Infections, Northwest Med. **33**: 200 (June) 1934.
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spond magically to treatment, and encephalitis,[6] septicemia due to Escherichia coli,[13] postabortional sepsis,[14] puerperal sepsis,[15] double septicemia,[16] pelvic cellulitis,[17] and biliary disease [18] have all been favorably influenced, according to the reports. It was estimated by Knott that approximately 45,000 treatments had been given between 1928 and 1948.

Gradually, factors in addition to those mentioned were suggested as responsible for the beneficial effect of ultraviolet irradiation of blood. The most important of these were (1) the increased phagocytic capacity of the polymorphonuclear leukocytes, (2) the increase in the oxygen combining value of venous bloods, (3) the breaking up and dispersal of the blood fat clumps or chylomicrons present in toxic patients, and (4) the return to normal of the lost Brownian movement of lipid particles.

DESCRIPTION OF APPARATUS

The apparatus known as the Knott hemo-irradiator

. . . consists of a self-contained, water-cooled, ultraviolet generator and an electrically driven transfusion pump and exposure device that mechanically controls the rate of flow and exposure of the blood to the rays. The apparatus can be accurately controlled as to the amount of ultraviolet generated as well as the time exposure of the blood to the ultraviolet ray. Between the source of the ultraviolet rays and the blood irradiation chamber there is a revolving shutter that subjects the blood to intermittent exposure to the rays. . . .

The keystone of Knott's instrument is a circular irradiation chamber

. . . approximately 2 inches in diameter and about 1 inch thick. The inside of the chamber has a labyrinthian passage connecting the inlet and outlet formed by baffle plates that are ground to fit flush against the quartz window forming the top of the chamber. Thus the blood must flow through the labyrinth by passing around one end of each baffle plate. The labyrinth is approximately 1 cm. deep. The irradiation chamber is so designed as to provide maximum turbulence of the blood in order to prevent the formation of a film on the chamber window that would absorb and filter out . . . ultraviolet and insure that all parts of the blood are equally exposed. . . .

HEMOIRRADIATION PROJECTS

Our own investigations with the Knott hemo-irradiator may be divided into three purposes: (1) the measurement of the physical attributes of the lamp used for irradiating the blood, (2) the evaluation of the sterilizing efficacy of the apparatus, and (3) the appraisal of its clinical effectiveness in two separate series of cases of varied diagnoses. The first study included 51 patients, and the second, 17. In this appraisal we were searching, in particular, for objective changes, especially hematologic changes of either morphologic or functional nature.

Measurement of Physical Qualities of the Lamp.[19]—The lamp submitted to us was an ultraviolet mercury lamp with a 250 watt alternating current burner. Measurements with phototubes at 2 cm. distance gave the following results: 4 milliwatts energy below 2,800 A.; 12 milliwatts energy between 2,800 A. and 3,800 A.; approximately 10 milliwatts energy in visible light; approximately 8 milliwatts energy in infrared. The total ultraviolet emission at 2 cm. is therefore approximately 16 milliwatts, and about 10% of this is in the spectral band of 2,537 A. The energy output of ultraviolet rays is considerable, but the emission in the sterilizing range of 2,537 A. or below is relatively low. Furthermore, the quartz plate, which is 2 mm. thick, absorbs approximately 10% of the ultraviolet energy. As a sterilizing lamp, therefore, the Knott hemo-irradiator is not an efficient burner.

Evaluation of Sterilizing Effect.—For the determination of the sterilizing effect, clear human plasma was seeded with Aerobacter aerogenes and then passed through the machine at the recommended rate of 30 cc. per minute. The rate of flow under these conditions is such that the plasma is exposed to the emanations of the burner for a total of six seconds. The bacterial count of the unirradiated plasma was 10,400,000 per cubic centimeter and of the irradiated plasma 1,500,000, a reduction by about 85%. In another experiment 3.5 liters of plasma was irradiated. This was done to determine whether deposits due to photochemical changes on the plate would make the plate less permeable to penetration by ultraviolet rays. In this experiment the unirradiated plasma contained 5,000,000 A. aerogenes per cubic centimeter, and the residual count at the completion of irradiation was 2,100,000, a reduction by only 60%. The quartz plate, after 3.5 liters of plasma had passed through the cell, showed an ultraviolet absorption of approximately 25%, instead of the 10% for the clean plate, which explains the diminished sterilizing capacity.

Preliminary Appraisal in Fifty-One Cases: First Study.—Our studies encompass the clinical and hematologic experiences with two groups of patients. The first hemoirradiation project, in which the Knott hemo-irradiator was used, was undertaken in September, 1949, and concluded in May, 1950. This group comprised 51 patients. They received 243 ultraviolet irradiations, with 1 to 33 treatments per patient. The amount of blood irradiated per treatment was 1.5 cc. per pound (3 cc. per kilogram) of body weight, not exceeding 200 cc. routinely; however, four patients had 500 cc. of blood irradiated on one or more occasions to permit us to determine whether this would have any deleterious clinical or

7. Miley, G.: Ultraviolet Blood Irradiation Therapy (Knott Technic) in Non-Healing Wounds, Am. J. Surg. **65**: 368 (Sept.) 1944.

8. Miley, G.: The Knott Technic of Ultraviolet Blood Irradiation in Acute Pyogenic Infections: Study of 103 Cases with Clinical Observations on Effects of New Therapeutic Agent, New York State J. Med. **42**: 38 (Jan. 1) 1942.

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18. Olney, R. C.: Ultraviolet Blood Irradiation in Biliary Disease: Knott Method, Am. J. Surg. **72**: 235 (Aug.) 1946.

19. Dr. Franz Oppenheimer performed the studies on the physical properties of the lamp.

hematologic effects. There were no demonstrable beneficial or harmful effects.

Hematology: The hematologic studies included erythrocyte, leukocyte, differential, platelet, reticulocyte, and eosinophil counts; sedimentation rates and hematocrit determinations; and bleeding and coagulation times. These tests were made routinely before the beginning of the treatments, on the day of each treatment, and at the conclusion of the treatment series. Two patients were checked daily for one week after the first treatment; five patients were checked every other day for two weeks; and several were examined at half-hour intervals for one and a half hours, then hourly for four hours following treatment. In three cases blood was removed for study from the tube leading to the irradiation chamber before exposure and again from the tube leading away from the chamber after irradiation. No significant blood changes were revealed by these studies.

Diagnostic Groups: Twelve diagnostic groups of patients with the following conditions were chosen for treatment: 23 with infectious hepatitis, 8 with stasis ulcers, 7 with arthritis, 2 each with acute rheumatic fever, pneumonitis, thrombophlebitis, and acute leukemia, and 1 each with lymphosarcoma, chronic brucellosis, sickle cell anemia with leg ulcers, atypical hemolytic anemia with leg ulcer, and herpes zoster.

Infectious hepatitis. In the group with infectious hepatitis frequent liver profile studies as well as physical examinations were made. All patients with hepatitis were at bed rest in the hospital during the treatments and received high protein, high vitamin diets. Three volunteered the information that they felt better after the treatments. None was made worse. The liver profiles were checked periodically, and all, including the controls, showed improvement. The group with hepatitis presented an unusual opportunity in a controlled experiment. The patients were chosen from a large group of young men who presumably had the same source of infection, the disease having been spread in the group by the use of unclean, contaminated needles during a "heroin party." One patient of the group with hepatitis received seven treatments in which all the steps of the irradiation procedure were performed, but the shutter was kept closed to exclude the ultraviolet rays from the blood. There was no demonstrable difference.

Stasis ulcers. In the group with stasis ulcers, one patient was at bed rest in the hospital, whereas the others were ambulatory. Four reported subjective improvement and decrease in pain, and in five the ulcers decreased in size during treatment. In the hospitalized patient, the ulcers almost completely healed but recurred when he increased his activity even though the treatments were continued. Five patients eventually discontinued treatment of their own accord.

Acute rheumatic fever. Subjective improvement occurred in both patients with acute rheumatic fever. The sedimentation rate was unaffected in either. Both were at bed rest in the hospital.

Pneumonitis. Neither of the two patients with pneumonitis was in the hospital long enough for evaluation.

Brucellosis. The patient with brucellosis was not clinically benefited, and the treatments were eventually stopped because of complicating hepatitis.

Lymphosarcoma. The case of lymphosarcoma was most instructive and emphasizes the difficulty of clinically evaluating the efficacy of the hemoirradiation method. The patient had a subjective feeling of well-being after almost all treatments but occasionally reported nervousness. This patient received 33 treatments with 10 control irradiations interspersed among them. During these 10, the entire procedure was performed, but the shutter was kept closed in order to exclude the ultraviolet rays from contact with the blood. The patient was never told that from time to time this would be done and assumed that all treatments were similar. Her subjective response to both control and regular treatments was the same. She felt stronger, "more alive," and invigorated by the procedures and was disturbed when they were discontinued. At no time, however, was there any objective evidence of either clinical or hematologic improvement.

Table 1.—*Summary of Data in First Study (Fifty-One Patients)*

	No. of Patients	Maximum No. of Treatments per Patient	Minimum No. of Treatments per Patient	Average No. of Treatments per Patient	Maximum Days from First to Last Treatment	Minimum Days from First to Last Treatment	Average Days from First to Last Treatment
Infectious hepatitis	23	9	1	4.12	42	0	15.7
Stasis ulcers	8	18	1	6.5	147	0	53
Arthritis	7	11	1	5.7	66	0	31
Acute rheumatic fever	2	10	8	9	37	33	35
Pneumonitis	2	2	1	1.5	3	0	..
Thrombophlebitis	2	2	1	1.5	3	0	..
Acute leukemia	2	2	2	2	4	4	4
Lymphosarcoma	1	33	..	....	241	..	..
Chronic brucellosis	1	8	..	....	34	..	..
Sickle cell anemia with leg ulcers	1	7	..	....	29	..	..
Atypical hemolytic anemia with leg ulcer	1	2	..	....	3	..	..
Herpes zoster	1	12	..	....	1	..	..

Miscellaneous. The patients with sickle cell anemia and leg ulcers, atypical hemolytic anemia with leg ulcers, and herpes zoster showed no improvement.

Summary of First Study: The number of control experiments was deliberately limited, because only positive results needed control and only subjective responses needed evaluation. A general summary of the number of treatments and the duration of the cause of treatments in the several diagnostic groups is given in table 1.

Evaluation of Second Hemoirradiation Project.—In July, 1950, the blood irradiation project was resumed by the Hematology Department of Cook County Hospital. The second series included a total of 17 patients with diagnoses of rheumatoid arthritis (2 patients), thrombo-

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phlebitis (1 patient), rheumatic fever (2 patients—one with chorea), and pelvic inflammatory diseases (12 patients).

The total number of treatments was 62, averaging almost 4 per case. Although the number of cases in each group was small, in no one case was any objective improvement noted. Many patients stated that they felt better, regardless of whether the drawn blood was irradiated (table 2).

TABLE 2.—*Summary of Data in Second Study (Seventeen Patients)*

Patient	Age, Yr.	No. of Treatments	Amount of Blood Irradiated, Cc.	Clinical Diagnosis	Remarks
H. T.	59	8	120-200	Thrombophlebitis with ulcer, chronic, 3 yr., acute 1 week; varicose veins	No improvement objectively; lesions continued to weep
B. M.	49	5	100-200	Arthritis, 6 mo.	No improvement subjectively or objectively
F. E.	41	4	200	Arthritis, 2 yr.	Subjective improvement; at no time was there limitation of movement
L. S.	6	7	105	Acute rheumatic fever;* before treatment, systolic and diastolic mitral murmur; enlarged heart; sedimentation rate 30; heart block (1 degree)	After first treatment sedimentation rate rose to 44; after third, severe nosebleed requiring packing; after fourth, mitral and aortic regurgitation diagnosed; sedimentation rate 30; after sixth, sedimentation rate 38, heart rate 104; after seventh, heart block (1 degree) persisted
M. McC.	8	8	105	Acute rheumatic fever and chorea, 2 weeks	Apical systolic murmur; x-ray: early mitralization; EKG normal; sedimentation rate after first treatment 15, after third 41, after sixth 23; no significant changes in heart sounds or x-ray
M. L.	38	2	150-200	Pelvic inflammatory disease, 1 mo. duration; fibroid uterus	Cramping pain in right lower abdominal quadrant; cervical discharge; no objective improvement
R. S.	32	3	120-150	Pelvic inflammatory disease 1 week's duration	Subjective improvement after first treatment; objectively no change; pain persisted after third treatment
J. D.	33	3	200	Pelvic inflammatory disease 3 weeks' duration	Lower abdominal pain; received sulfonamides 3 days and penicillin once; chills, fever continued; generalized tenderness; Bartholin abscess; acute bilateral salpingitis; blood not irradiated first two treatments (temperature elevated); blood irradiated third time, temperature down to 98 F and increased later in day; septic temperature persisted; operated on for pelvic abscess
L. F.	38	3	200	Pelvic inflammatory disease	Received no antibiotics; pain in abdomen 1 day; adnexae bilateral diffuse induration; blood not irradiated with first treatment, but subjectively and objectively better; subjectively and objectively improved after third treatment; no further vaginal discharge; no other medication
L. H.	34	2	100	Pelvic inflammatory disease and fibroid uterus	Received penicillin once before irradiation and felt better; painless; no objective improvement
L. B.	23	1	200	Chronic pelvic inflammatory disease, exacerbation 8 days, rebound tenderness all quadrants; vaginal discharge	Signed release before final evaluation possible
N. M.	?	1	100	Subacute exacerbations, pelvic inflammatory disease 4 days; tenderness and rigidity both lower abdominal quadrants; Bartholin abscess	Discharged after first treatment; subjectively improved
V. M. J.	19	3	200	Pelvic inflammatory disease	Abdominal cramps, discharge, chills, fever, one day; tenderness in both lower abdominal quadrants; after first treatment severe abdominal pain; given penicillin once; 3 days later process subsided; subjective improvement; objectively slightly improved at completion of treatment
R. R.	?	3	150	Acute pelvic inflammatory disease	No antibiotics; abdominal pain 2 weeks, localized to left lower quadrant day of admission; rebound tenderness bilaterally; subjective improvement after third treatment; objectively, adnexa tender and thickened; mass in left cul de sac; pyosalpinx
H. P.	?	3	100-150	Recurrent bilateral pelvic inflammatory disease; lower abdominal pain 28 hours; adnexa bilaterally tender; foul sanguinomucoid discharge	No irradiation; no antibiotics; after first treatment pain lessened; objectively somewhat improved; marked thickening of adnexae; some tenderness on movement of cervix; at end of third treatment left adnexa: retort-shaped mass, slightly tender; pyosalpinx
H. R.	34	3	200	Pelvic inflammatory disease	Subjective improvement; objectively pelvic findings unchanged; mass appeared in right adnexa during treatment
T. C.	21	3	150	Gonococcic infection; acute pelvic inflammatory disease	Blood not irradiated; after treatments pains severe, then subsided in two days; no subjective or objective improvement

* Treated also with acetylsalicylic acid.

CONCLUSIONS

We have concluded that none of our patients derived benefit from the irradiation of blood with the Knott hemo-irradiator. These are at best, however, preliminary results. We do not feel that, on the basis of our observations, definitive conclusions can be drawn. It can, however, be categorically stated that, in both series studied by us, the first of 51 cases and the second of 17, no dramatic clinical or reproducible objective changes, which could be attributed to the irradiation treatments rather than the natural variation in the course of the disease or to psychic effects, could be demonstrated. On the other hand, no adverse effects were noted. A longer and more extensive program of study is warranted before in vivo ultraviolet irradiation of blood can be finally either accepted or rejected.

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DEVELOPMENT OF PROTEUS AND PSEUDOMONAS INFECTIONS DURING ANTIBIOTIC THERAPY

Ellard M. Yow, M.D., Houston, Texas

Within recent months antimicrobial agents capable of suppressing the multiplication of almost all of the pathogenic bacteria have been given widespread clinical trial. None of these agents has been effective against all strains of the Pseudomonas (Pyocyaneus)[1] and Proteus group of organisms. As the result of the suppression of other more pathogenic bacteria in the prophylactic or therapeutic use of the antibiotics, these relatively nonpathogenic organisms have frequently been allowed to multiply and have played an active part in the pathogenesis of infectious processes.

It is the purpose of this paper to present examples of infections due to Proteus or Pseudomonas that developed during or following therapy with the commonly used antimicrobial agents. During the past two years 56 patients have been observed with such infections. Their diagnoses are presented in the table and eight illustrative cases are described. The pathogenesis, diagnosis, and treatment of these infections are also discussed.

REPORT OF CASES

CASE 1.—A 53-year-old chronic alcoholic was admitted to the hospital because of chills, fever, cough, and chest pain. The symptoms began four days before admission and progressed in spite of penicillin therapy. On physical examination there was evidence of consolidation of the lower lobe of the left lung. The liver was enlarged. On admission the white cell count was 5,250, with a predominance of polymorphonuclear leukocytes showing toxic granulations. Sputum and throat cultures revealed Klebsiella pneumoniae. X-ray studies confirmed the clinical findings of pneumonia of the base of the left lung posteriorly.

The patient was treated (fig. 1) with penicillin, dihydrostreptomycin, aureomycin, and chloramphenicol (chloromycetin®). He gradually improved, and by the fourth day of therapy K. pneumoniae could not be cultured from the sputum, the leukocyte count had risen to 18,650, and his temperature had gradually decreased. On the seventh day the patient appeared somewhat worse. The following day his condition appeared markedly worse, and he became disoriented. At this time, x-ray and physical examination revealed evidence of a spread of the pneumonia in the lower lobe of the left lung as well as involvement of the lower lobe of the right lung. Cultures of the sputum revealed Pseudomonas aeruginosa in pure culture, except for an occasional colony of Candida albicans (Monilia). The patient's condition became progressively worse in spite of an increase in the dose of dihydrostreptomycin.

In vitro sensitivity tests indicated that the strain of Pseudomonas was resistant to penicillin, streptomycin, chloramphenicol, and aureomycin, but inhibited by 1.9 μg per milliliter of polymyxin B. The antibiotics being administered were discontinued as the patient was given polymyxin B intramuscularly in doses of 50 mg. every six hours. Within 48 hours the patient began to improve, and there was gradual subsequent resolution of the pneumonia, decrease of the fever, and reestablishment of the normal flora of the sputum. On the eighth day of polymyxin therapy the dose was reduced to 25 mg. every six hours. The drug was continued for a total of 15 days, during which results of daily examinations of the urine and blood and determinations of blood urea nitrogen and urinary output were normal except for occasional traces of albumin. The patient made an uneventful recovery and has remained well.

CASE 2.—A 42-year-old woman who worked as an office supervisor had had diabetes since 1927, but had otherwise been well until December, 1949. During the Christmas holidays of that year she had an acute upper respiratory tract infection complicated by a purulent sinusitis. She was treated with penicillin and irrigations intermittently for a month. On the first of February she developed chills and fever, with urinary frequency and burning. She was found to have pyuria and was treated for two days with aureomycin. She improved and returned to work, but the following day there was a recurrence of symptoms. She responded to aureomycin therapy again but in a few days relapsed. During the next month there were eight episodes of urinary infection, which responded to aureomycin but recurred when it was discontinued. The ninth course of aureomycin failed to control elevation of temperature and urinary symptoms, and the patient was referred to a urologist. She was treated with penicillin and streptomycin with improvement. Three weeks later there was a return of the symptoms, and she was admitted to the hospital.

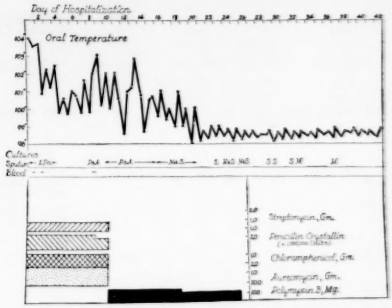

Fig. 1 (case 1).—Course of a 53-year-old chronic alcoholic who was admitted for treatment of Friedländer's pneumonia. After initial improvement, the pneumonia progressed, and Ps. aeruginosa was cultured from the sputum.

Physical examination at this time revealed a chronically and severely ill patient. The liver was slightly enlarged, and there was bilateral costovertebral angle tenderness. Laboratory examinations revealed a moderate leukocytosis and a slight hypochromic anemia. The urine contained albumin (2+), sugar (4+), many white blood cells, and gram-negative bacilli. The blood urea nitrogen level was 107 mg. per 100 cc. Ps. aeruginosa was repeatedly isolated from the urine and blood. The patient was given sulfonamides, methenamine mandelate (mandelamine®), streptomycin, and chloramphenicol without improvement (fig. 2).

Beginning the first of July the patient received polymyxin B intramuscularly in doses of 50 mg. every four hours for 24 hours, followed by 25 mg. every four hours. The blood culture

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This article has been shortened by omission of figures 2, 3, and 7. They will be included in the author's reprints.

From the Department of Internal Medicine, Baylor University College of Medicine, and the Ben Taub Infectious Disease Laboratory, Jefferson Davis Hospital.

This study was supported in part by a grant from Burroughs Wellcome and Company, Inc., Tuckahoe, N. Y., and the polymyxin B (aerosporin®) sulfate used in this study was supplied by Dr. Donald S. Searle, Medical Director.

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on the first day after beginning polymyxin B injections was negative and a decrease in the number of bacteria in the urine was recorded; however, cultures of the urine remained positive. Administration of polymyxin B was continued for 10 days, during which the patient's temperature returned to normal and she improved generally. She complained of numbness and tingling of her hands and face and pain at the site of the injections. These symptoms disappeared after discontinuing the drug. At the be-

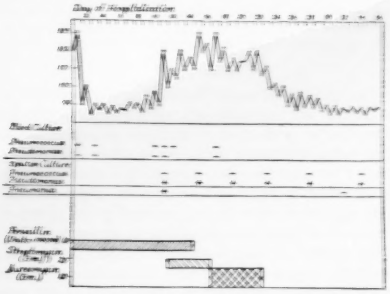

Fig. 4 (case 4).—Course of a 27-year-old woman with Pseudomonas pneumonia following pneumococcal bacteremia.

ginning of polymyxin therapy the urine contained albumin (3+). The amount of albumin in the urine decreased during treatment. At the termination of polymyxin B therapy the urine was not entirely free of pus cells, and the cultures were not sterile. On the second day after discontinuing the drug the fever returned and the abnormalities in the urine progressed. The patient was subsequently explored surgically, and multiple kidney abscesses were found and aspirated. She was then given terramycin with gradual but complete recovery.

CASE 3.—A 78-year-old man when first seen was comatose. An acquaintance stated that he had apparently been well until about a month previously, when urinary frequency had developed. He was given antibiotics with initial improvement, but while he was still receiving these drugs chills and fever developed. About a week before admission a productive cough developed. Examination revealed an emaciated and chronically ill man with a fever of 105 F, pulse rate of 128, and respiratory rate of 28. There were rales in both lung bases, but the remainder of the physical examination was noncontributory. The white cell count was 4,300, with 50% polymorphonuclear leukocytes; urinalysis revealed a slight trace of albumin, with 5 to 8 white blood cells per high power field. The blood urea nitrogen level was 51 mg. per 100 cc. Administration of penicillin was begun shortly after admission without improvement (fig. 5). He was subsequently given aureomycin and later streptomycin. Proteus vulgaris was isolated repeatedly from the blood and urine. This organism was found to be inhibited in vitro by 31.2 μg. of chloramphenicol per milliliter, but resistant to other antibiotics tested. He was subsequently given 0.5 gram of chloramphenicol in acetyl dimethylamine, intramuscularly, every four hours. Blood levels varying between 20 and 50 μg. per milliliter were reached with temporary improvement in the patient's condition. While he was taking the drug, however, the bacteremia returned and he died on the 13th hospital day.

CASE 4.—A 27-year-old Negro woman who was a chronic alcoholic was admitted to the hospital because of chills and fever. Physical examination was noncontributory. Her temperature was 103 F. The white blood count was 12,800, with 84% polymorphonuclear leukocytes. Pneumococci were isolated from the blood stream. The patient was treated with penicillin, with a prompt control of the fever and bacteremia (fig. 4). On the ninth day of penicillin therapy the fever returned, and there was clinical and x-ray evidence of pneumonia of the base of the right lung. Beginning with the 11th hospital day, the predominant organism repeatedly isolated from the sputum was Ps. aeruginosa. The penicillin was discontinued, and streptomycin and aureomycin were substituted. There was no definite evidence of the beneficial effect of antibiotic therapy. The patient improved gradually and was afebrile by the 30th hospital day. There was slight residual evidence of pneumonia at discharge.

CASE 5.—A 61-year-old salesman had been found to have an adenocarcinoma of the lung and was admitted to the hospital for pneumonectomy. Prior to and following the operation, the patient was given penicillin (fig. 5). Following the operation he developed a bronchopleural fistula and empyema. Cultures of the empyema fluid contained a mixed flora, including Streptococcus hemolyticus, Micrococcus pyogenes, and species of Hemophilus and Neisseria. There was a gradual rise in temperature in spite of the administration of penicillin. On the 10th postoperative day administration of streptomycin was begun and two days later aureomycin was added. There was a prompt improvement. The fever returned, however, and Ps. aeruginosa was isolated from the pleural fluid. The previous therapy was discontinued, and on the 20th postoperative day polymyxin B was given intramuscularly (50 mg. every six hours) and intrapleurally (25 mg. daily). The patient improved slightly, but he continued to have a low grade fever and the chest continued to drain. The number of Pseudomonas colonies cultured from the chest fluid decreased with polymyxin B therapy, but the organism was not entirely eliminated. During the second week of therapy the cultures of the chest fluid revealed staphylococci and hemolytic streptococci. The patient's condition gradually deteriorated, and he died on the 47th hospital day. During the administration of polymyxin B there was no evidence of nephrotoxicity except for occasional mild albuminuria. There was, however, a terminal rise in the blood urea nitrogen to 76 mg. per 100 cc., which was considered to be prerenal and not related to the drug therapy. An autopsy was not performed.

CASE 6.—An 18-year-old youth was admitted to the hospital because of hydrocephalus that had developed following a skull injury four years previously. A diagnostic pneumoencephalogram was complicated by purulent meningitis. This infection responded promptly to sulfadiazine, penicillin, and streptomycin. An operation was subsequently performed, anastomosing the subarachnoid space with the left ureter. In spite of prophylactic administration of penicillin and sulfisoxazole (gantrisin*), a spiking fever and purulent spinal fluid developed three days following the operation (fig. 6). Cultures of the spinal fluid revealed P. vulgaris; Esch. coli, P. vulgaris and Pseudomonas

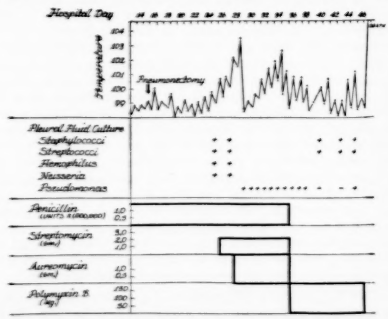

Fig. 5 (case 5).—Course of a 61-year-old man with postoperative empyema.

aeruginosa were isolated from the urine. The doses of the penicillin and sulfisoxazole were increased, and, when there was no improvement, streptomycin and chloramphenicol were added. There was no response to either of the antibiotics, and on the 23rd postoperative day polymyxin B was given intramuscularly (50 mg. every six hours) and intrathecally (2 mg. daily). The patient improved promptly and on the fourth day of therapy the intrathecal administration of polymyxin B was discontinued. The intramuscular dose of polymyxin B was reduced to 25 mg. every six hours the following day and discontinued after 10

days of therapy. The patient made an uneventful recovery. During the polymyxin B therapy the patient had no complaints, and results of daily urinalyses were normal except for slight albuminuria and pyuria that had been present prior to therapy. At the beginning of polymyxin therapy the blood urea nitrogen level was 23 mg. per 100 cc., but during therapy it returned to normal. This patient was discharged on the 60th postoperative day without evidence of recurrence of infection.

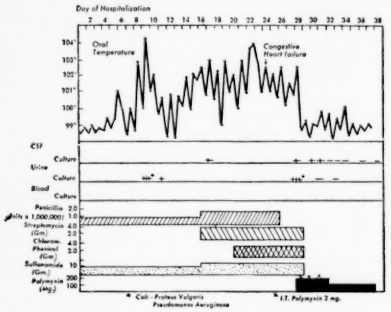

Fig. 6 (case 6).—Course of an 18-year-old youth with postoperative meningitis due to P. vulgaris.

CASE 7.—A 54-year-old Mexican was admitted to the hospital because of acute urinary retention. He had been in the hospital previously for an abdominoperineal resection for adenocarcinoma of the colon. At this time he was given prophylactic phthalylsulfathiazole (sulfathalidine®), penicillin, and streptomycin before and following the operation. On admission he had a low grade fever and was given penicillin and streptomycin (fig. 7). In spite of this treatment the temperature rapidly rose to 105 F by the sixth hospital day. Urine cultures revealed a mixed infection, including Aerobacter aerogenes, Esch. coli, Streptococcus hemolyticus, P. vulgaris and Ps. aeruginosa. Blood cultures were sterile. Penicillin and streptomycin were continued and on the eighth hospital day, terramycin was added to the regime. There was rapid clinical improvement, and a transurethral resection was performed on the 22nd hospital day. The following day there was a sharp rise in temperature and P. vulgaris was isolated from the blood stream. In addition to continuing administration of penicillin and streptomycin, administration of terramycin was again begun on the 23rd hospital day. There was no clinical improvement, and blood cultures were consistently positive for Proteus vulgaris. The penicillin dosage was increased and sulfithoxazole was added. On the 28th day the patient developed cutaneous petechiae and had two subsequent pulmonary infarctions. In vitro sensitivity tests indicated that this strain of Proteus was resistant to penicillin, streptomycin, and terramycin, but relatively sensitive to chloramphenicol (inhibited by 31.2 μg per milliliter). He was consequently given chloramphenicol but had congestive heart failure and died two days later. Autopsy revealed bilateral pyelonephritis, generalized carcinomatosis, and pulmonary congestion and infarctions.

CASE 8.—A 61-year-old publisher was admitted to the hospital with chills and fever, urinary frequency, and burning. He had had previous episodes of acute urinary infections that had responded to either sulfonamides, penicillin, streptomycin, or aureomycin. In addition, he had arteriosclerotic heart disease with a recent myocardial infarction and congestive heart failure. Urinalysis on admission revealed albumin (4+), many white blood cells, and occasional red blood cells. The white blood cell count was 26,000 per cubic millimeter. The blood urea nitrogen level was 12 mg. per 100 cc. Ps. aeruginosa was cultured from the urine and blood. He was treated with sulfithoxazole and aureomycin without improvement (fig. 8). On the fourth hospital day intramuscular injections of polymyxin B were begun (50 mg. every six hours). Ps. aeruginosa was not cultured from the urine after the fifth hospital day, and blood cultures became negative. On the fourth day of therapy the temperature had returned to normal, and the dose was reduced to 25 mg. every six hours. The following day a transurethral prostatic resection was performed. Administration of polymyxin B was continued for a total of 11 days, during which time the pyuria disappeared, the albuminuria varied from 1+ to 4+, and the urinary output and blood urea nitrogen remained within normal limits. No evidence of recurrent infection occurred during this hospitalization. The patient was discharged on the 18th hospital day.

COMMENT

The patients discussed illustrate what is believed to be an increase in relative importance of Proteus and Pseudomonas in the production of infectious processes that may arise during antibiotic treatment of other infectious diseases. Clinical experience suggests that there might also be an actual increase in frequency of infections due to these organisms since the introduction of the agents with the broadest antimicrobial spectra. In an analysis (fig. 9) of the routine cultures received in the bacteriology laboratory of a large general hospital, the incidence of Proteus in the specimens received rose from 8% of the gram-negative bacilli recovered in June, 1948, to 32% in January, 1951. During the same time the incidence of Pseudomonas recovered increased from 15% to 30%. These data also reflected the clinical experience reported by others of the increase in the frequency of infections due to Candida (Monilia).[3] During the same period of two and one-half years there was a relative decrease in the isolation of certain other gram-negative bacilli, particularly Esch. coli. One cannot conclude from these figures that there has been an actual increase in clinical infections due to Proteus and Pseudomonas, since they are based on laboratory reports and not individual patients. The results of this study indicate, however, that these organisms are oftener present in body fluids or exudates and may serve as potential sources of infections.

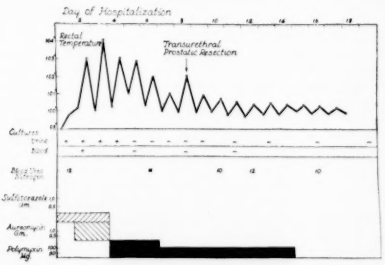

Fig. 8 (case 8).—Course of a 61-year-old man with an acute urinary infection previously treated with antibiotics. Ps. aeruginosa was cultured from the urine.

The isolation of Proteus or Pseudomonas from a patient does not necessarily mean that either of these organisms is playing a significant role in the production of an infectious process, since they are both normal inhabitants of the skin and the mucous membranes of the respiratory and gastrointestinal tracts. If the organisms are isolated in pure culture repeatedly from body fluids that are normally sterile, such as the blood stream, spinal fluid, or

3. Woods, J. W.; Manning, I. H., Jr., and Patterson, C. N.: Monilial Infections Complicating the Therapeutic Use of Antibiotics, J. A. M. A. **145**: 207 (Jan. 27) 1951.

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urine, in the presence of clinical evidence of infection, there can be little doubt as to their significance. When they are obtained in mixed infections or from skin secretions or mucous membrane surfaces, it may be difficult to evaluate their importance. However, if there is clinical and laboratory evidence of progressive infection

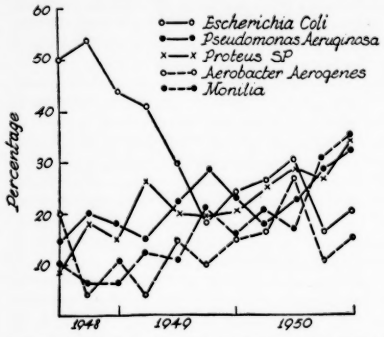

Fig. 9.—Analysis of results of routine cultures in a large general hospital illustrating the relative frequency of some of the gram-negative bacilli.

and either of these two organisms is isolated in pure culture or as a predominant organism the importance of their role in pathogenesis must be strongly considered and their control undertaken.

The relationship of the infections to the antimicrobial therapy was thought in most patients to be simply a matter of the elimination of sensitive species of bacteria, permitting the multiplication of resistant species. Since Proteus and Pseudomonas are usually the only bacteria surviving the action of the most recently introduced antibiotics, they are frequently the only remaining etiological possibilities. There was, moreover, a disturbance of some fundamental defense mechanism against infection in many of the patients. In some of the patients the infections resulted from anatomical defects prevented the adequate drainage of contaminated material. Urinary infections associated with prostatic or ureteral obstructions were frequently observed. Bronchiectasis and undrained abscesses are other examples. In other patients infected material was introduced into a closed body space, such as by puncture wounds of the bowel or chest either from trauma or operation, or by the contamination of the cerebrospinal fluid.

The onset of the signs and symptoms of the Proteus and Pseudomonas infections frequently occurred after a period of improvement following suppression of the initial etiological agent. This is illustrated by the patient (case 1) with cirrhosis of the liver in whom a Friedländer's pneumonia developed. This improved with the institution of massive antibiotic therapy, but later the pneumonia spread in spite of continued therapy. In case 4 pneumonia developed due to Pseudomonas while the patient was still receiving penicillin that had controlled pneumococcal bacteremia.

The course of the Proteus or Pseudomonas infections was quite variable. The correction of the underlying anatomical defect and surgical drainage was frequently adequate to control the infection. Other patients were able to develop sufficient immunity to overcome the infection when the antibiotic therapy was discontinued and the normal bacterial flora reestablished. The administration of specific antibacterial agents sometimes played a significant role in shortening the course of the infection. In four patients no therapy was effective and the infection contributed to a fatal outcome.

An important factor in controlling the infections studied was establishment of adequate surgical drainage and removal of nonvital tissue. In urinary tract infections, particularly, antibiotic therapy usually produced only transient benefit if adequate urinary drainage was not achieved. The extent of the surgery necessary varied considerably. Needle aspiration was sufficient drainage in a patient with septic arthritis. In postoperative empyema extensive surgical drainage in conjunction with streptokinase and streptodornase administration was necessary in some cases.

When a particular strain of Proteus or Pseudomonas was found to be sensitive in vitro to one of the antibiotics, the administration of this agent was found to play a valuable part of the management of the infection. Because of the wide variation in sensitivity of Proteus and Pseudomonas to antibiotics, in vitro sensitivity tests were routinely performed as an aid in selecting the agent of choice. The results of such in vitro tests using the tube dilution method against 50 strains of Pseudomonas are illustrated graphically in figure 10. These findings illustrate generally the resistance of Pseudomonas to most of the antibiotics as contrasted to the high degree of sensitivity to polymyxin B. The chart does not, however, present an entirely accurate picture, since some of the strains tested were isolated from patients who had already received one or more of the antibiotics, thus eliminating some of the more sensitive strains from the survey. Furthermore, the arbitrary test level of 15.6 μg per milliliter indicating sensitivity in this table may not entirely parallel the results in patients, since this drug level may not be attained in the infected tissues and body fluids. The study indicates, however, that the largest number of strains of Pseudomonas were sensitive in vitro to polymyxin B. Many were also sensitive to terramycin and neomycin.

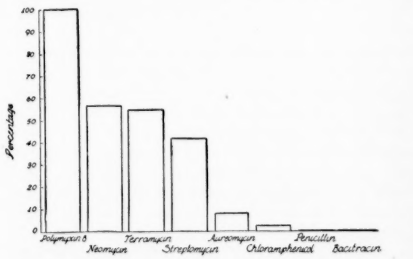

Fig. 10.—The in vitro sensitivity of 50 strains of Pseudomonas to various antibiotics at a concentration of 15.6 μg per milliliter.

A similar study was performed using 20 strains of Proteus. Many of these organisms were partially inhibited by the antibiotics against which they were tested, but only an occasional strain was completely inhibited by

concentrations of the drugs obtained in the body fluids by the usual dosage schedules.

A summary of the results of the antibiotic therapy in the 56 cases reported in this series reveals that polymyxin B was the most effective agent in the treatment of Pseudomonas infections. In the nine patients in whom it was used, the infections were satisfactorily controlled in seven, or 78%. In contrast to reports following the use of less pure preparations, there was no evidence of significant toxicity noted from the use of this antibiotic. Terramycin and streptomycin exerted a favorable influence on the course of the infection in an occasional patient. Neomycin was not evaluated clinically because of other reports of toxicity following parenteral administration. Antibiotics played a less significant role in the treatment of the Proteus infections. Two patients with polymyxin-sensitive strains responded to the use of this drug. Streptomycin, given with large doses of one of the sulfonamides, is probably still the best treatment for infections due to this organism.

Number of Patients in Whom Pseudomonas or Proteus Infection Developed During or Following Antibiotic Therapy

Infection	No. of Cases	
	Pseudomonas	Proteus
Bacteremia	4	2
Pulmonary infections	5	0
Empyema	4	0
Meningitis	3	1
Peritonitis	0	1
Arthritis	1	0
Urinary infections	19	15
Prostatitis	1	0

SUMMARY

The suppression of the other bacteria by the widespread use of antimicrobial agents has increased the relative importance of Proteus and Pseudomonas as causative agents in infectious processes. Cases of infections due to these organisms that developed during or following repeated courses of antibiotic therapy are reported. The relationship of the infection to the antibiotic therapy was believed in most patients to be a matter of change in bacterial flora owing to elimination of sensitive bacteria and multiplication of resistant species. The importance of being aware of the possibility of Proteus or Pseudomonas infections in patients who originally respond to antibiotic therapy but who present evidence of renewed infection while still receiving therapy is illustrated by the patients described. The possible seriousness of giving the broad spectrum antibiotics prophylactically must be considered, since if an infection does occur with a nonsensitive organism during such therapy, it is almost certain to constitute a difficult therapeutic problem.

The problem of treatment of Proteus and Pseudomonas infections is considered. Streptomycin in combination with large doses of sulfonamides was the most effective therapy in Proteus infections. Polymyxin B was most consistently effective in Pseudomonas infections, though some strains were sensitive in vitro to terramycin. The correction of any underlying anatomical disorder was considered a most important part of management. The discontinuance of ineffective antibiotics was sufficient in some patients to control the infection by allowing the reestablishment of normal bacterial flora.

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THERAPEUTIC VALUE OF PROBENECID (BENEMID®) IN GOUT

Luke R. Pascale, M.D., Alvin Dubin, M.S.
and
William S. Hoffman, M.D., Chicago

Probenecid (benemid®) was first introduced into clinical medicine by Boger [1] as an adjunct to penicillin and paraaminosalicylic acid therapy. Probenecid has been found to be a powerful agent that reversibly inhibits renal tubular transfer, suppressing tubular secretion of penicillin, paraaminosalicylic acid, paraaminohippuric acid, and phenolsulfonphthalein.[2] In this respect it is similar to carinamide; but while the latter is required in doses of 18 to 24 gm. per day for its tubular effect, probenecid accomplishes the same results in doses of 2 gm. daily. That probenecid, like carinamide, is also capable of blocking tubular reabsorption of glomerular constituents was demonstrated by Schneider and Corcoran,[3] who were able to increase the excretion of phosphate by administration of the drug. Gutman, acting on the report by Wolfson and associates [4] that carinamide was a uricosuric agent, demonstrated that probenecid had a similar effect, presumably by blocking the partial reabsorption of filtered urate. A preliminary report by Gutman on the efficacy of probenecid in the treatment of gout has recently appeared.[5] Bishop and associates [6] also reported a uricosuric activity of probenecid but with no clinical studies.

The similarity of action of probenecid to that of carinamide led us independently to study the potential value of this new drug in the treatment of gout. Our studies were begun without benefit of the experiences of Gutman and Bishop. In these studies, after a preliminary demonstration of the uricosuric action of probenecid, an effort was made to determine an adequate dose schedule in the treatment of gout, the extent of improvement in patients with gouty arthritis, and the possible toxicity from prolonged administration.[7]

Mrs. Anne Whittier made the chemical analyses for this study.
Presented in part before the Central Society for Clinical Research, Chicago, Nov. 2, 1951.

From the Hektoen Institute for Medical Research of the Cook County Hospital, the Department of Medicine, Stritch School of Medicine, Loyola University (Dr. Pascale), and the Department of Physiology, University of Illinois College of Medicine (Dr. Hoffman).

1. Boger, W. P.; Beatty, J. O.; Pitts, F. W., and Flippin, H. F.: The Influence of a New Benzoic Acid Derivative on the Metabolism of Para-Aminosalicylic Acid (PAS) and Penicillin, Ann. Int. Med. **33**: 18-31 (July) 1950. Boger, W. P.; Pitts, F. W., and Gallagher, M. E.: Benemid and Carinamide: Comparison of Effect on Para-Aminosalicylic Acid (PAS) Plasma Concentration, J. Lab. & Clin. Med. **36**: 276-282 (Aug.) 1950.

METHODS AND MATERIALS

The 20 male subjects for this study were ambulant or bed patients of the Cook County Hospital. The diagnosis of gout was established in all these patients by the history or observation of typical acute gouty attacks and by the finding of elevated serum uric acid concentration. In seven patients there was the additional evidence of tophi and/or diagnostic x-ray changes. Limitation of joint motion was seen in these seven as well as in four other subjects. In four subjects the limitation was severe, in five it was moderate, and in the remaining two it was mild. Ten of the patients were under observation for periods of five to seven and a half months. Six more were followed for two to five months. Four patients were dropped from the study after the preliminary survey.

The demonstration of the uricosuric effect of probenecid therapy was carried out in the first five patients studied. The subjects were placed on a standard low purine diet. After a control period, probenecid was prescribed in doses of 0.5 gm. (one tablet) every six hours. The 24-hour urine collection and the serum were analyzed for uric acid by a photoelectric modification [8] of the Folin method. (Since the values were comparative, no effort was made to eliminate the nonspecific chromogen by the use of uricase. Wolfson and associates [9] have shown that true urate of serum and urine in gouty patients consistently represents 85% to 90% of the apparent urate. The range of serum concentrations in normal persons by this method was 3.0 to 5.9 mg. per 100 cc.) With increased excretion of urate and a fall in the serum urate level, probenecid therapy was discontinued to allow a return to pretreatment conditions. Then the experiment was repeated.

Several regimens were tried out in most of the patients. These included administration of 2 gm. of probenecid daily, 2 gm. every other day, and 2 gm. for only two successive days out of each week. In three patients the effect of acetylsalicylic acid simultaneously administered with probenecid for four days was compared with that of probenecid therapy alone. During the later part of the study five patients were not given probenecid and treated with 5.2 gm. of acetylsalicylic acid and 8 gm. of sodium bicarbonate daily for three weeks. The administration of 2 gm. of probenecid daily was then resumed.

A standard low purine diet was used only for the patients hospitalized for the urine studies, chiefly to assure a constant purine intake. During the period of the various maintenance regimens, the patients were allowed a more or less general diet.

The possible toxicity of probenecid was studied by weekly physical examinations and frequent blood chemical analyses. The latter included the determination of nonprotein nitrogen, albumin, globulin, calcium, phosphorus, alkaline phosphatase, chloride, sodium, potassium, carbon dioxide capacity, cholesterol, cephalin cholesterol flocculation, and thymol turbidity. Also, at frequent intervals complete blood cell counts were made and routine urine examinations performed.

Uric Acid Clearances Before and During Probenecid Therapy in Gouty Patients

	Before Probenecid Therapy				During Probenecid Therapy			
Patient	Serum Uric Acid, Mg./100 Cc.	Urine Uric Acid, Mg./100 Cc.*	Volume of Urine, Cc./Min.*	Uric Acid Clearance, Cc./Min.	Serum Uric Acid, Mg./100 Cc.†	Urine Uric Acid, Mg./100 Cc.*	Volume of Urine, Cc./Min.	Uric Acid Clearance, Cc./Min.†
G. R.	8.5	18.9	1.4	3.1	4.8	23.5	1.5	7.3
H. S.	9.0	28.8	1.8	5.8	4.8	24.5	1.7	8.7
O. B.	11.2	50.1	0.9	4.0	7.8	65.3	1.2	10.5
F. C.	14.1	34.2	1.2	2.9	6.7	60.0	1.4	12.5
H. Sp.	9.3	23.0	2.1	5.2	7.4	27.9	2.3	8.7

* Based on 24 hour output.
† Uric acid clearances were determined on the third or fourth day, after stabilization of serum uric acid levels had occurred.

RESULTS

Effect of Probenecid on Urinary Urate Excretion and on Serum Urate Level.—An increase in urinary excretion of urate occurred promptly in 17 of the 20 patients studied. In the five subjects of whom protracted quantitative studies were made, the increase was equivalent to 35% to 200% of the control excretion. In some instances the 24-hour urine contained 1.5 to 2.4 gm. of urate. Much of it was already precipitated in the collection bottle. The initial high excretion was not maintained. Gradually it fell, corresponding to the lowering of the serum uric acid concentration (fig. 1). The pattern of excretion was similar to that reported by Gutman [5] and by Bishop and associates.[6] The roughly estimated 24-hour urate clearances were increased two to fourfold by the administration of probenecid (see accompanying table). This increased clearance was still effective during the diminished excretion, the latter merely reflecting the fall in serum uric acid concentration. Though continuous quantitative collections of the urine were carried out only in the first phase of the study, occasional 24-hour analyses gave us the impression that the daily excretion of urate during administration of probenecid was always higher than that of the control period, at least in the patients with tophaceous gout, just as was found by Gutman.

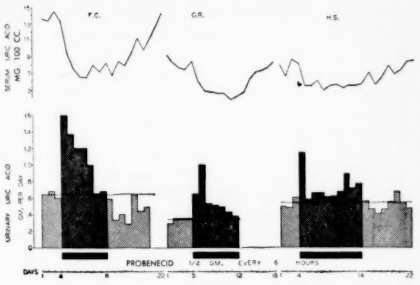

Fig. 1.—Effect of probenecid on urinary uric acid excretion and serum uric acid levels.

A prompt precipitous fall in the serum urate concentration occurred in 14 subjects, as illustrated in the cases shown in figure 1. Three patients showed a more gradual fall in serum levels, the nadir not being reached until 96 or 120 hours. In three other subjects no decrease in the serum uric acid level occurred, even though 2 gm. of probenecid was administered daily for one to three weeks. The failure was apparently associated with the renal

2. Beyer, K. H.: Functional Characteristics of Renal Transport Mechanisms, J. Pharmacol. & Exper. Therap. **99**: 227-280 (Aug.) 1950.

3. Schneider, R. W., and Corcoran, A. C.: Familial Nephrogenic Osteopathy Due to Excessive Tubular Reabsorption of Inorganic Phosphate: A New Syndrome and a Novel Mode of Relief, Proceedings of the Central Society for Clinical Research, vol. 23, 1950.

4. Wolfson, W. Q.; Cohn, C.; Levine, R., and Huddlestun, B.: Transport and Excretion of Uric Acid in Man, Physiologic Significance of the Uricosuric Effect of Carinamide, abstracted in Am. J. Med. **4**: 744 (May) 1948.

5. Gutman, A. B.: Some Recent Advances in the Study of Uric Acid Metabolism and Gout, Bull. New York Acad. Med. **27**: 144-164 (March) 1951.

6. Bishop, C.; Rand, R., and Talbott, J. H.: The Effect of Benemid (p-[di-n-propylsulfamyl]-benzoic acid) on Uric Acid Metabolism in One Normal and One Gouty Subject, J. Clin. Investigation **30**: 879 (Aug.) 1951.

7. Sharpe & Dohme, Inc., supplied the probenecid used in this study.

8. Hoffman, W. S.: Photelometric Clinical Chemistry, New York, William Morrow & Co., 1941.

9. Wolfson, W. Q.; Huddlestun, B., and Levine, R.: The Transport and Excretion of Uric Acid in Man: The Endogenous Uric Acid-Like Chromogen of Biological Fluids, J. Clin. Investigation **28**: 995-1001 (Sept.) 1947.

insufficiency discovered in these subjects. Two had urea clearances of 26% and 27% of normal, respectively, and the third had chronic azotemia with nonprotein nitrogen levels ranging from 68 to 85 mg. per 100 cc. These three unresponsive patients were not studied beyond the three-week period.

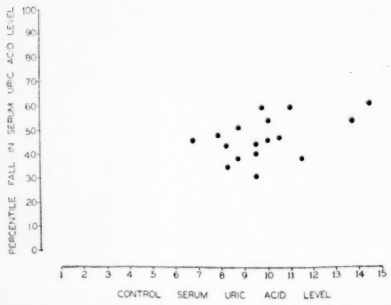

Fig. 2.—Relation of percentile fall in serum uric acid levels after 72 hours of probenecid therapy to the control (pretreatment) serum uric acid levels, in milligrams per 100 cc.

The percentile fall in the serum urate level at the end of the 72 hours in the 17 subjects who responded to probenecid therapy ranged from 30% to 58%, the average fall being 45%. In some instances a lower serum level was encountered several days later, but for the most part the serum concentration rose slightly with continued probenecid therapy and was maintained at a level slightly higher than that of the nadir. There was no significant correlation between the percentile fall and the height of the control serum urate concentration (fig. 2).

In the five patients who were given 2 gm. of probenecid daily for only the first two days of each week, the initially lowered serum uric acid level was not maintained; instead, there was a rapid rise during the next five days to the pretreatment levels. With each new two-day period of probenecid administration, the serum uric acid level fell as promptly as before. Though in several instances the extent of the fall with each new treatment period appeared to be slightly less than previously, there were no instances of developed refractoriness to probenecid therapy. Figure 3 is illustrative of the curves obtained.

During the course of the study 16 subjects were maintained on a regimen of 2 gm. of probenecid given every other day for periods ranging between 4 and 15 weeks. The response to this dosage varied unpredictably. Four patients, within the first two weeks, had a slow but steady rise in serum uric acid concentration above the initially obtained minimal level. In four more, a rise eventually occurred but was delayed for 6 to 10 weeks. In the remaining eight patients, though an initial rise might temporarily have occurred, the depressed serum uric acid level was on the whole well maintained during the 4 to 15 weeks of observation. However, all the patients who were again given 2 gm. of probenecid daily showed a further depression of the serum uric acid concentrations. There was no doubt that, insofar as serum levels were concerned, the most satisfactory regimen was a dosage of 2 gm. of probenecid daily given continuously. For greater convenience the medication schedule was 1 gm. given twice a day instead of 0.5 gm. given every six hours, without any appreciable change in the serum levels. With this continuous therapy the uric acid concentration could be maintained indefinitely at levels ranging from 4 to 8 mg. per 100 cc., with occassional temporary rises, especially at times of an acute attack.

One of the 20 patients in this study died suddenly of coronary occlusion after preliminary daily treatment with probenecid for four weeks. He was 76 years old. Autopsy revealed no anatomic defects that could be related to the administration of probenecid.

Effect of Probenecid on the Symptoms of Gout.—In figure 4 are summarized the pertinent clinical data of the 16 patients who were treated with probenecid for an extended period. The eight patients who displayed limitation of joint motion all showed progressive improvement during probenecid therapy. G. R., a barber with gout for five years, had not been able to work more than three days a week, if at all, during the past three years because of stiffness and pain in the joints of the extremities. After six weeks of probenecid therapy he became completely relieved of pain and joint dysfunction and is now working at his trade six full days per week, with continued medication. O. B. had been completely bedridden for a period of one year because of gouty arthritis. This lesion was superimposed on a residual paralysis of the right lower extremity and weakness of the left foot resulting from poliomyelitis. After five months of probenecid therapy, he was able to walk with the aid of his brace and crutches as well as he did before the onset of gout. J. B. had been bedridden two months with continued pain and severe limitation of joint movement. At the end of three months of probenecid therapy he was able to walk unaided and to drive his automobile. Five other patients showed comparable, if less dramatic, improvement. Of this group, H. P. and P. K., both of whom had large tophaceous deposits in the hands, showed the least benefit from treatment, but even in these two there was enough improvement, both objective and subjective, to make them enthusiastic over the treatment and desirous of its continuation.

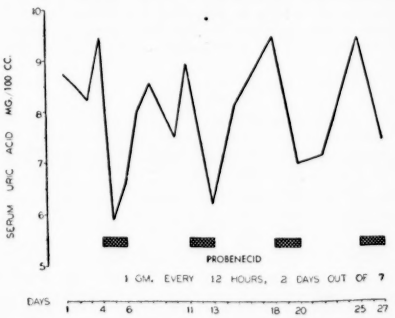

Fig. 3.—Serum uric acid levels in patient receiving intermittent probenecid therapy.

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In the eight patients with acute recurrent gout without symptoms in the intercritical periods, the results of therapy were, of course, more difficult to evaluate. The serum uric acid was maintained in these persons at levels only slightly higher than the upper limits of normal without any restrictions of diet. This was an important benefit in

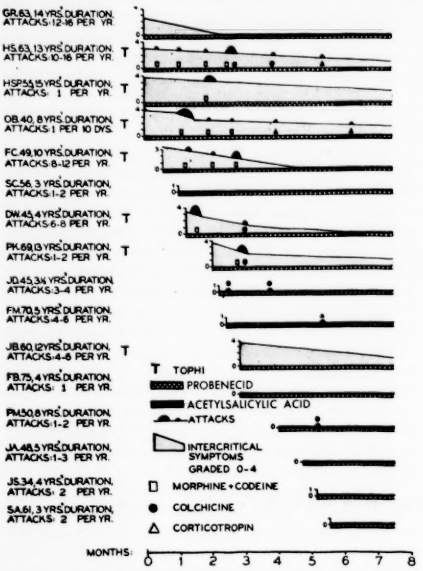
GR.63, 14 YRS. DURATION, ATTACKS: 12-16 PER YR.
HS.63, 13 YRS. DURATION, ATTACKS: 10-16 PER YR.
HSP.55, 15 YRS. DURATION, ATTACKS: 1 PER YR.
OB.40, 8 YRS. DURATION, ATTACKS: 1 PER 10 DYS.
FC.49, 10 YRS. DURATION, ATTACKS: 8-12 PER YR.
SC.56, 3 YRS. DURATION, ATTACKS: 1-2 PER YR.
DW.45, 4 YRS. DURATION, ATTACKS: 6-8 PER YR.
PK.69, 3 YRS. DURATION, ATTACKS: 1-2 PER YR.
JD.45, 3½ YRS. DURATION, ATTACKS: 3-4 PER YR.
FM.70, 5 YRS. DURATION, ATTACKS: 4-6 PER YR.
JB.60, 12 YRS. DURATION, ATTACKS: 4-6 PER YR.
FB.75, 4 YRS. DURATION, ATTACKS: 1 PER YR.
PM.50, 8 YRS. DURATION, ATTACKS: 1-2 PER YR.
JA.48, 5 YRS. DURATION, ATTACKS: 1-3 PER YR.
JS.34, 4 YRS. DURATION, ATTACKS: 2 PER YR.
SA.61, 3 YRS. DURATION, ATTACKS: 2 PER YR.
T TOPHI
PROBENECID
ACETYLSALICYLIC ACID
ATTACKS
INTERCRITICAL SYMPTOMS GRADED 0-4
MORPHINE + CODEINE
COLCHICINE
CORTICOTROPIN
MONTHS
0 1 2 3 4 5 6 7 8

Fig. 4.—Clinical course of 16 patients with gout during probenecid therapy.

itself. The patients felt well and had no complaints, but patients with recurrent gouty attacks usually acted that way even without medication. Three of these patients had acute attacks during the period of medication. J. D. had a moderately severe attack after six days of probenecid therapy, which lasted four days; then he had a mild attack four weeks later, which lasted two days. P. M. had one attack during the three and a half months of therapy, and F. M. had one mild attack after three months of therapy. The remaining five patients were free of acute manifestations of gout during the therapeutic study; but, since they normally had only two or three attacks a year, a much more prolonged study will be required to ascertain the effect of probenecid therapy on the incidence of acute joint manifestations.

The fact that one or more attacks occurred in nine patients during probenecid therapy is an important physiological as well as therapeutic problem. Gutman [5] has reported the same phenomenon, and he has attributed the attacks to the action of probenecid. This may be the case, but it is far from certain. The attacks occurred principally in those patients who had had them frequently before probenecid therapy and who had chronic gouty arthritis with multiple urate deposits. In the first attacks we were courageous enough to continue probenecid therapy and to avoid the use of colchicine or corticotropin (ACTH). Only codeine or morphine were utilized for the pain. As a consequence, the attacks were rather prolonged, some lasting 12 days. It was obvious that probenecid had no colchicine type of action. It neither relieved the acute pain nor shortened the length of the attack. With the subsidence of the inflammation in the acutely involved joint, there was usually less limitation of motion in that joint than before the attack. D. W., for example, before the first attack in his left knee during probenecid therapy, had had only 80 degree flexion of the knee joint. After the attack subsided, he was able to bend the knee 135 degrees, or practically normally. Succeeding attacks in the same patient usually migrated to other joints.

The frequency and intensity of acute attacks in the patients with chronic gouty arthritis appeared to diminish with continued probenecid therapy, as is seen in figure 4. When it was finally recognized that probenecid therapy was of no value for the acute attacks, subsequent episodes were managed with colchicine or corticotropin [10] therapy. The former was given in doses of 0.65 mg. (1/100 grain) every four hours until diarrhea set in. Corticotropin was used in four attacks in doses of 10 mg. every six hours; two to four injections were required. Whether colchicine or corticotropin was used, the attacks usually subsided completely in 24 to 72 hours.

Effect of Salicylate on the Uricosuric Action of Probenecid.—It is well known that sodium salicylate or acetylsalicylic acid given in large doses has a uricosuric effect and that with prolonged administration a lowering of the serum urate level is produced in gouty subjects. It was interesting, therefore, to determine the influence of acetylsalicylic acid administered simultaneously with probenecid. To our surprise, acetylsalicylic acid given in

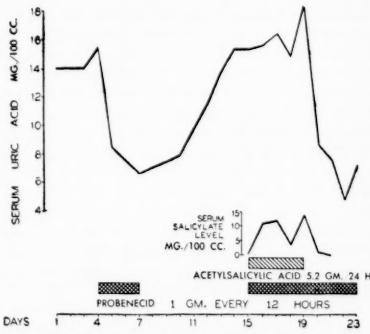

Fig. 5.—The influence of acetylsalicylic acid therapy on the ability of probenecid therapy to lower the serum uric acid concentration.

doses of 1.3 gm. every six hours completely suppressed the effect of probenecid. The blood urate remained at least as high as without any medication. When acetylsalicylic acid therapy was stopped after four days, while probenecid therapy was continued, the fall of the serum uric acid was just as prompt and as precipitous as in

10. The corticotropin used was furnished by the Wilson Laboratories, Chicago.

previous probenecid therapy. Identical results were seen in the three patients in whom this effect was studied. One experiment is shown in figure 5.

The fixation of the serum uric acid level when acetylsalicylic acid was given along with probenecid was almost certainly due to a blocking of the uricosuric action of probenecid. It could not be due to falsely high serum uric acid levels, because of the presence of salicylates or its metabolites in the blood. We have made innumerable determinations of uric acid in gouty and nongouty patients during salicylate therapy and have never found any false elevation of serum uric acid. However, to prove conclusively that salicylates exert their influence by preventing the uricosuric effect of probenecid and to determine at what threshold serum salicylate level this inhibition occurs, it is necessary to carry out urine urate analyses. One must take special precautions in analyzing urine for urate during salicylate therapy, for it has been shown [11] that gentisic acid, a metabolite of salicylate, may on occasion raise the apparent urine urate concentration by as much as 25% even when the uricase method of analysis is utilized. Such studies are now in progress.

Some of the five patients were maintained for a period of three weeks on a regimen of 1.3 gm. of acetylsalicylic acid and 2 gm. of sodium bicarbonate given four times a day for five out of each seven days. The serum uric acid concentration rose in all these patients from the low level of the previous probenecid regimen to the high control levels. Slowly the concentration diminished in two of these patients, but it never fell to the level found in the probenecid therapy period.

Toxic Effects of Probenecid Therapy.—On the whole the patients remained remarkably free of side-effects of probenecid therapy. Only three patients had changes that could be attributed to toxicity due to probeneicd. H. S. had a rash, which disappeared without recurrence in spite of continued probenecid therapy. During his only gouty attack while receiving treatment, proxysmal auricular fibrillation developed. This arrhythmia was converted to normal by digitalization. The rhythm has since then remained of sinus origin. J. A. had epigastric distress, which subsided after two days despite continued therapy.

The one potentially serious complication occurred in O. B. This was the development of urate crystalluria and hematuria early in the course of treatment with probenecid. Treatment with the drug was temporarily stopped, and the complications disappeared within two days. After eight days, probenecid therapy was resumed and was supplemented with administration of sodium bicarbonate and an increased water intake. There was no recurrence of the urinary findings.

Blood chemical analyses showed no significant deviations from normal that might indicate renal or hepatic injury or disturbances of electrolyte metabolism. Serum phosphate levels were at low normal. Since the data of the chemical analyses were not enlightening, they have been omitted. Complete blood cell counts made serially gave no evidence of inhibition of normal erythropoiesis and granulopoiesis or of any other abnormality. There were no alterations found in the urine on repeated routine examinations, except for heavy urate precipitations when the specimens were allowed to stand.

COMMENT

Gout is still a mysterious disease, the etiology and pathogenesis of which have not been unraveled; yet modern investigations point to three fundamental features of the gouty patient that must be understood if the potentialities of probenecid therapy are to be appreciated:

1. Gout occurs in patients with familial hyperuricemia.[12] The cause of the elevated serum uric acid level has not been determined, but it may be (*a*) overproduction of uric acid, (*b*) diminished destruction of uric acid, or (*c*) diminished renal excretion of uric acid. In the last analysis, it is absolute or relative renal inefficiency that is responsible for the hyperuricemia. for the normal urate clearance is only 5% to 10% of the glomerular filtration rate, a large portion of the filtered urate being reabsorbed by the tubules by active enzymatic processes.[13] The system of the gouty patient, instead of adjusting excretion by diminishing tubular reabsorption, attempts to do so by raising the level of serum uric acid.

2. Hyperuricemia is attended by actual or potential supersaturation of urate in the interstitial fluids, at least in special sites, such as around joints, in bursae, and in cartilage. Thus hyperuricemia ultimately defeats its own purpose. With precipitation of urates in the tissues, the serum level should fall. However, a renewed high level is soon established to maintain excretion, which level allows further precipitation. Repeated waves of positive balance of uric acid are thereby produced by the very hyperuricemia designed to avoid this eventuality. From the work of Benedict and his associates [14] with isotopic uric acid, it appears that the freshly precipitated urate is in the form of fine crystals that are easily redissolvable and are part of the miscible pool of uric acid. The older deposits, however, particularly the material in the depth of tophi, are chalky and much less soluble. This portion is not in equilibrium with the soluble or dissolved urate.

3. The gouty patient has a unique exaggerated inflammatory reaction to precipitation of urates in the region of the joints, associated with severe pain, swelling, and limitation of motion. This reaction is promptly reversible by the administration of colchicine or corticotropin, without relation to any change in the excretion of urate.[5] The fact that gouty patients even during intercritical periods have low excretions of 17-ketosteroids,[15] the fact that the administration of small quantities of corticotropin is effective in reversing such attacks, and the fact that gouty attacks are induced by all the stresses that are known to call for an increased production of adrenocortical hormones and by administration of corticotropin followed by its withdrawal,[16] all point to a disturbance in adrenal function in gouty patients.

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Probenecid therapy attacks the problem of gout at the level of renal excretion. It does nothing for the specific gouty response to urate deposition; it merely removes the hyperuricemia. Probenecid is apparently the most effective and most harmless uricosuric agent so far discovered. It is far more effective than neocinchophen or acetylsalicylic acid, without the attendant dangers of these drugs. It produces a large negative balance of uric acid when first administered at a time of high serum uric acid levels, and a continued small negative balance when the serum level has been lowered to near the upper limit of normal. Gutman has estimated an extra excretion of about 75 gm. in five months. Though we have been unable to carry out prolonged urine collections to determine this excretion, extrapolations from our limited data would tend to confirm Gutman's estimation.

The therapeutic value of the negative uric acid balance produced by probenecid was unequivocal in the patients with chronic tophaceous gout. The disability was diminished in all cases and almost completely removed in several. Apparently the urate that is first removed is in the form of easily soluble crystals loosely deposited around the joints and on the surface of old tophi. Benedict and associates [14] have demonstrated that as much as 29 gm. of such miscible urate deposits can be removed in three months by the uricosuric effect of acetylsalicylic acid. The rate of removal with probenecid therapy is undoubtedly greater.

Benedict and his associates have called attention to the fact that the removal of urate deposits by acetylsalicylic acid in their case was accomplished without a significant lowering of the serum uric acid level. However, it has been our experience both in the several weeks of acetylsalicylic acid therapy in the present series of cases and in long-term studies in other cases that the serum uric acid level does slowly fall with continued acetylsalicylic acid therapy. Nevertheless, it is undoubtedly true that administration of acetylsalicylic acid does not produce the rapid fall in serum level accomplished with probenecid therapy. Apparently the uricosuric effect of probenecid therapy is so great that excretion is always ahead of resorption of deposited uric acid, whereas in the case of acetylsalicylic acid therapy the excretion is slow enough to allow solution to keep pace with it, as long as an appreciable store of easily miscible urate is available. Eventually, as the miscible pool shrinks, the excretion becomes slightly faster than solution, and the serum uric acid level slowly declines.

It was impossible in the short period of the present study to evaluate the effective probenecid therapy on recurrent nontophaceous gout. Nevertheless, it is fair to prophesy that, with continued therapy and with the maintenance of the serum levels near the range of normal, tophi will be prevented from forming and that eventually acute gouty episodes will seldom occur. Of course, such an eventuality will depend on the innocuousness of continued probenecid therapy over a long period.

It is possible, though far from certain, from our data and from those of Gutman that acute attacks are precipitated shortly after the beginning of probenecid therapy, at least in patients with chronic tophaceous gout. The mechanism of this development in the presence of a much lowered serum uric acid level is difficult to visualize. Perhaps solution of urates takes place in one region while reprecipitation takes place in another region, where local factors (which might be characteristic of gout) are conducive to disturbances of the supersaturated solution. At any rate it is our clinical impression that these attacks are not likely to occur in the same joint again with continued probenecid therapy and that the rate and intensity of recurrence ultimately diminishes. Certainly, with the recognized efficiency of colchicine and/or corticotropin therapy in alleviating the acute episodes, this circumstance should prove no contraindication to probenecid therapy.

The blocking effect of acetylsalicylic acid on the uricosuric action of probenecid was unexpected. If salicylates act, as Levine and associates maintain,[17] by freeing serum urate from its combination with serum protein, this annulling effect should not occur, whether probenecid owes its uricosuric effect to a similar liberation of urate from protein or whether it acts by interfering with tubular reabsorption of urate. Indeed, one should expect a synergistic effect. In consideration of the recognized action of probenecid in preventing tubular excretion of penicillin and paraaminosalicylic acid, it appears unreasonable to look elsewhere than in the tubules for the uricosuric effect of probenecid.

Salicylate probably exerts its interference with the action of probenecid directly in the tubules. It has been demonstrated [18] that, unless the urine is strongly alkaline, 50% to 80% of ingested salicylate or acetylsalicylic acid is excreted as salicyluric acid or salicyl glycuronide. Almost all of this conjugation takes place in the renal tubules. If we assume that probenecid produces its blocking action on urate reabsorption only after it is conjugated in the tubular cell, then it is possible to visualize the negating effect of salicylate as being due to its competition with probenecid in the tubule for the conjugating enzymes. This hypothesis is not out of accord with Beyer's theory of tubular transport mechanism.[2]

Obviously we have not been able to explore all possible dosages of probenecid. On the basis of previous experience with probenecid in penicillin and paraaminosalicylic acid therapy, we have kept the daily dosage at 2 gm. per day, but have varied the days of treatment, hoping to find a less rigorous management than daily administration satisfactory. Though we could see no clinical difference between the dosage of 2 gm. of probenecid given every day and that of 2 gm. given every other day, it was clear that in only a few patients—usually those without tophi—could the serum urate level be kept relatively low without continuous therapy.

The possibility of the development of hematuria from uric acid crystals or calculi must be seriously considered. We have recognized the phenomenon in only one patient, but we may have overlooked transient episodes in other patients. When the initial uric acid level is very high—12 to 15 mg. per 100 cc.—the daily excretion may be of the order of 2 gm. This quantity of urate, even in urine volumes of 2,000 cc., is far too great to be held

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in solution at the usual pH of urine.[19] Therefore, we have recommended a large fluid intake and the ingestion of about 8 gm. of sodium bicarbonate daily during probenecid therapy. When the initial serum uric acid level is very high, it is probably safer to begin treatment at 1 gm. of probenecid per day. However, we have had no experience with that dosage.

The failure of probenecid therapy to lower the serum urate level in three patients with diminished renal function must be further explored in both gouty and nongouty patients. It is important to determine whether renal insufficiency was actually the cause of failure of probenecid action in these cases and, if so, what the nature and degree of the renal defect must be to cause this failure. Such experiments are now being carried out.

SUMMARY

The therapeutic potentialities of probenecid in the treatment of recurrent gout and chronic gouty arthritis were studied in 20 patients. Ten were followed for periods of five to seven and a half months. With a dose of 2 gm. daily, serum uric acid fell within 72 hours to an average of 55% of the control level. This was associated with an initial increase in urate excretion of 35% to 200%. Urate clearances remained increased two to fourfold with continued probenecid administration.

In three patients with decreased renal function, probenecid therapy produced no fall in the serum uric acid level. When acetylsalicylic acid was given simultaneously with probenecid, the action of the latter in lowering the serum uric acid level was completely annulled but was restored when acetylsalicylic acid therapy was discontinued.

Probenecid therapy proved of greatest benefit in chronic gouty arthritis. Joint movement improved progressively in all patients; pain and swelling subsided. Acute attacks of gout developed in some patients soon after treatment was started, but their incidence diminished with continued therapy. No significant or consistent changes occurred in the serum electrolyte concentrations during prolonged therapy. No abnormalities in blood cell distribution were found. Results of hepatic and renal function tests remained normal. In one patient mild hematuria occurred from urate crystals during the first stage of treatment.

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BLUEPRINT FOR IMPROVED PHYSICIAN-PATIENT RELATIONS

Chester L. Roberts, M.D., Glendale, Calif.

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The public is becoming impatient with the physician who is merely a good technician. Years ago, the patient had a beloved family physician to whom he could take all of his problems, medical and personal. Today, advances in medical and surgical methods assure the patient of improved physical treatment, but he often finds that he is no longer treated as an individual with a disease but as a "case" of a certain disease. Worse still, if the patient suffers from one of the many conditions that cause bothersome, disabling aches and pains that cannot be analyzed medically nor classified definitely into one category or another, the illness is too often considered to be psychosomatic.

Every patient who seeks medical help for the relief of painful symptoms is entitled to an unhurried and sympathetic hearing, whether his problems be primarily physiological, primarily psychological, or a combination of the two. Patients with organic problems are often in need of a strong dependable relationship, a framework within which reassurance can be offered to offset or alleviate the anxiety aroused by the patient's fears. On the other hand, patients whose symptoms are mildly or markedly excessive in view of the physical findings often experience a great deal of relief in sharing emotional problems with their physicians.

Beginnings of the relationship between the physician and the patient are laid even before the initial contact with the physician. The impress of the physician's personality can be felt the moment the patient steps into the reception room. Favorable first impressions are most important.

OFFICE MIRRORS THE PHYSICIAN'S ATTITUDE

The patient should be regarded as a guest, not as an interruption of the receptionist's work. The receptionist, like all persons employed by the physician, will take her cue from her employer: if he apparently welcomes the patient's visit, the receptionist will do so; if the physician is annoyed at the interruption, that attitude is passed on by the girl at the front desk.

Someone should be on hand to greet each patient. The newcomer should be made to feel welcome; he should be smiled at and spoken to cordially, by name if he has been in before. If the patient's name is foreign or difficult to pronounce, the receptionist should record the correct pronunciation of the name on the folder or card for the physician's use and for future reference. Use of the patient's name shows recognition and appreciation.

The patient should be given some idea of the probable wait before he can see the physician. If the physician has been called out, the patient should be informed of this, and the receptionist might suggest that the patient use the time for having coffee or shopping. If, for any reason, the physician will be unable to see the patient at the appointed time, every effort should be made to reach the patient at the earliest possible moment by telephone or even by telegram. The physician's staff should show that they and the physician appreciate the fact that the patient's time, too, is valuable.

The physician himself can do much to make the patients awaiting their turns in the reception room feel his friendly interest. A smile or nod in recognition and welcome as he catches sight of an old patient will ac-

complish wonders. A high degree of intelligence is needed to increase the patient's feeling of his own individuality and to convince him that his best interests are being respected. The physician should insist that the office nurse usher in patients in their turn, rich and poor alike. Patients should not be turned away because they have neglected to make appointments if they can be fitted into the appointment schedule.

Special provision should be made for the handling of exceptional patients, such as the patient with facial deformity who shuns contact with others, the patient who coughs and sneezes, the drunk or belligerent patient, and the talkative, forgetful, and argumentative elderly patient who needs kindly and tactful attention.

Patients expect a sense of reserve on the part of the physician and his employees. If the receptionist or office nurse gossips and discusses the idiosyncrasies of the man or woman who has just left the office, the patient receives the impression that the physician, too, is probably too talkative about his patient's concerns. If charts are left out in the open where they can be studied by all comers, and, if names are used loosely in telephone reports of laboratory or physical findings, patients are uneasy. Closed doors add to feelings of privacy. The waiting room serves as the physician's showcase, and the secretary or receptionist should be considered a mirror of the doctor himself.

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CONCEPT OF THE "PERSONAL PHYSICIAN"

Men in medical practice today fall into one of two categories: the specialist and the general practitioner. The specialist publicly announces his intention to limit his practice to some specialty, possibly to the study of one organ or one disease process. The general practitioner, on the other hand, purports to fill the place of the beloved old-time family physician—a family physician, however, with modern techniques and knowledge.

The public is confused by the multiplicity of medical specialities, yet it has come to think of the general practitioner as a medical drudge who can handle small, routine medical problems adequately but is hardly to be trusted with serious medical disease. The public has become very specialist minded.

Ernest Dichter, in his report to the Committee on Medical Economics of the California Medical Association, has suggested that the term "general practitioner," to which such disapprobation has attached, should be replaced by the concept of the "personal physician," a specialist in medical management whose job it is to administer, secure, and supervise the best available care for all medical and surgical problems. While the specialist limits his study to one disease or one organ, the personal physician gives his attention to the disease process in the whole person. Moreover, he sees the whole person operating in a specific family set-up and within a definite socioeconomic framework.

For example, the specialist, focusing his attention on the effects of tension and overwork on a single organ or group of organs might say, "Stop worrying. Go to a beach resort for a period of at least three months, and rest up." This advice, while practicable for patient A or B, may be wholly unrealizable when applied to patient C, who is barely able to support herself and her bedridden mother. The personal physician, knowing the circumstances, that a three month holiday is out of the question and that the suggestion would only add to the patient's distress and give her additional cause for worry, might suggest a more practical alternative in the light of the patient's situation, such as a rearrangement of work hours, frequent rest periods, week-ends in bed, and the like. Knowing the patient's background, the personal physician is able to sift his observations with shrewdness and judgment not always given to the specialist.

SYMPATHETIC HANDLING IMPORTANT

In the physician's inner sanctum, the physician-patient relationship is defined as the physician listens with calm, unhurried, and sympathetic attitude to the patient's version of the problem. The physician will often learn much in this way that he might miss in the more direct question-and-answer type of interview. Kindness and tactfulness are most important. It is not easy to be pleasant as one nears the end of a long day, but every patient needs good humor, sympathy and a quiet manner, no matter how weary or upset the physician may be personally. At times, high tension in the patient may be relaxed by a pleasant bit of conversation or a momentary diversion.

The physician should concentrate his entire attention on the patient during the consultation. His desk should be free from distracting material. If possible, he should refrain from answering the telephone while seeing a patient. Patients should receive special handling with reference to age and position. The older man expands in an atmosphere of respect and deference; the aging woman objects to any act that may emphasize her frailty. Adolescent youngsters object to being "treated like children."

Careful and efficient physical examination and performance of indicated laboratory procedures impart to the patient the feeling that a sympathetic and capable friend is in control of the situation. If the examination is made with authority and assurance, the procedure itself has psychotherapeutic value and the medications prescribed often acquire psychological meaning that increases their efficiency beyond their pharmacologic value.

A common criticism of the medical profession is that the physician does not explain the patient's illness to him. Explanations need not be lengthy or complicated. Simple explanations couched in terms the patient can understand and possibly accompanied by simple line diagrams, are sufficient. Explanations should include the following: (1) what the condition involves; (2) the chances of recovery; (3) the duration of hospitalization; (4) the length of convalescence; (5) the probable cost; and (6) how soon normal activities can be resumed. The patient should be invited to become an active participant in the whole treatment.

False hopes should not be aroused. Patients usually react to bad news more favorably than members of the family. If the patient's fears are unfounded, the physician should not laugh at the fears; he should explain them away instead. Patients whose symptoms cannot be explained by physical findings or who report symptoms out of all proportion to observable pathological conditions often make speedy recoveries after the nature of their illness is explained to them. Physicians should be slow to dismiss an illness as psychosomatic. Apparently psycho-

logical symptoms may arise from organic causes. Whether the patient's illness is primarily physiological or primarily psychological, the patient should receive the best aid possible.

"CALLING IN" THE SPECIALIST

Close cooperation between the specialist and the personal physician will assure the best care to the patient. In cases where the knowledge or technique of the specialist is of value, the personal physician should discuss the need for a specialist's care with the patient. The personal physician should act for the patient in choosing a specialist and then, rather than turn the patient over to the specialist, he should "call in" the specialist. To maintain continuity, the personal physician and not the specialist should conclude the case.

Thus the patient will be given a feeling of security and continuity of relationship. He will feel that the physician has a warm, friendly, and continuing interest in him. This feeling can be strengthened by a telephone call to the patient after the case has been concluded, inquiring as to the recovery of the patient.

FEES

Medicine should be placed on a business basis; this means that fees should be discussed in the initial interview. Each physician should have his own constant, self-determined fee schedule, based on his cost of doing business plus a reasonable profit. In setting up a fee schedule, the physician must bear in mind the range of fees customarily charged for the services in the area. He may decide that he prefers his fees to be among the higher fees charged or among the lower, but the fees set should fall within the customary range. If necessary, he must decrease his costs so that his fees can be kept within the accepted range.

The physician should never raise his fees because the patient is wealthy; his fee schedule should be revised only downward, in special instances. Financial return, although necessary, should be subordinated to humanitarian aims. Few physicians who enter medicine because they expect to receive a substantial income are successful.

The physician should acquaint himself with the community's resources, and he should make provisions for the care of indigent patients. He should be diplomatic in his referrals to such agencies, such as by referring to the foolhardiness of assuming an extra burden at the time, rather than laying stress on the charity aspects.

PLEASING PERSONALITY IMPORTANT

It is apparent that the physician must cultivate a warm, empathic relationship with his patients. He must learn to overlook his patients' faults and shortcomings and to appreciate their good points. He must become aware of the patient as a whole and as an individual, and he must cultivate a real interest in patients as persons.

Since his relations with his employees are reflected in the atmosphere of the office, the physician should make it a point to have an occasional word of appreciation if he always finds his rooms in readiness when he comes into the office, his mail in order and laid out with requested information clipped thereto. He must cultivate a good relationship with other physicians in the community, for his income is in part determined by referrals.

If the physician finds that he lacks the personality traits needed to succeed as a personal physician, he would be wise to affiliate himself with a medical group, a hospital, or a laboratory, where size of practice is not so dependent on personality.

606 N. Brand Blvd.

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DISEASE TRANSMISSION BY INEFFICIENTLY SANITIZED ANESTHETIZING APPARATUS

J. Mehsen Joseph, Ph.D., Toledo, Ohio

From observing the construction of an anesthetizing apparatus one would conclude that the soda lime tower is adequate for the removal of bacteria-laden droplets from the patient under treatment. Such is not the case, however, as was indicated in the study of the source of several cases of follicular tonsillitis in patients administered an anesthetic for surgical purposes; the anesthetizing apparatus was the disseminating agent.

In addition to the dissipation of disease, the administration of anesthetics will contribute to the invasiveness and production of disease by microorganisms. Dubin [1] found it easier to produce influenza virus pneumonia in anesthetized ferrets and mice than in similar animals that had not been anesthetized with ether. Andrews, Laidlaw, and Smith [2] noted that of six mice inoculated intranasally with human influenza virus without previous anesthetization only two showed gross pulmonary lesions while eight inoculated with the same suspension after ether anesthetization all showed severe pulmonary lesions. Shope's [3] work revealed two possible explanations. 1. Irritation of the respiratory mucosa by ether favored the establishment of the virus. 2. Owing to the inhibition of the sneeze reflex by the anesthetic a much larger dose was introduced more deeply into the respiratory tract.

Mote [4] suggests that ether in some way alters the physiological state of the respiratory mucosa making it more susceptible to the virus. This is probably manifested as an increase in the secretion of mucus, since Wheeler and Nungester [5] showed that the administration of atropine sulfate intraperitoneally into mice before the instillation of the influenza "A" virus decreased the ex-

From the Department of Bacteriology, University of Toledo.

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4. Mote, J. R.: General Consideration of Virus Diseases of the Respiratory Tract, Cambridge, Mass., Harvard University Press, 1940, p. 409.

5. Wheeler, A. H., and Nungester, W. J.: Effect of Atropine Sulfate on the Course of Influenza Virus Infections, Science **100**: 523, 1944.

tent of infection in these animals. Atropine sulfate is known to decrease the secretion of mucus by the respiratory mucosa.

One can reconcile the fact that anesthetics increase the susceptibility of patients to various respiratory diseases by their inhibitory or detrimental effect on some neurotropic viruses as reported by Sulkin, Zarafonetis, and Goth.[6] These authors concluded that diethyl ether alters the outcome of virus infections to a favorable extent; organisms inhibited in vitro are also inhibited in vivo. Bronfenbrenner and Weiss [7] noted a decrease in mortality in experimental botulism by employing ether anesthetic for varying periods of time as a therapeutic measure. Thus, it is apparent that, if an organism can pass to the rebreathing bag of an anesthetizing apparatus, disease transmission is highly favored.

EXPERIMENTAL METHODS

Studies were designed to determine the passage of microorganisms from the patient to the rebreathing bag, to isolate and identify species present, to establish disease transmission by anesthetizing apparatus, and to institute proper methods of sanitization.

TABLE 1.—*Bacterial Counts on Apparatus Immediately After Use and Without Sanitization*

Apparatus Tested	Total Bacterial Counts	
	Tube	Rebreathing Bag
A-1	420,000	345,000
A-2	200,000	368,000
A-3	1,000,000	648,000
A-4	2,205,000	736,000
A-5	3,400,000	530,000

Samples were taken from the tubes and the rebreathing bags of anesthetizing apparatus immediately after removal from the patients. This was effected by adding 250 cc. of sterile tap water to each tube and properly manipulating to remove as many organisms as possible; rinsings were collected in sterile flasks. Rebreathing bags were removed and thoroughly rinsed with 500 cc. of sterile tap water. Two types of controls were employed; one was an apparatus that had not been cleaned or used for several days, and the other was an anesthetizing apparatus immediately removed from the patient and thoroughly cleaned. Total counts were made on all samples by using the conventional dilution method. Various colonies appearing on the agar plates were transferred and properly numbered in order to maintain viability and identity. Isolated colonies were studied microscopically, culturally, and biochemically to establish their generic and species names. All organisms isolated were tested for hemolysis on blood agar, gram reaction, motility, spore formation, pigmentation, and colony type on nutrient agar. Reactions for triple sugar iron agar, desoxycholate agar, sugar broths, gelatin, nitrate, and IMViC for the organisms investigated were contingent upon the aforementioned reactions. This procedure provides data relative to the passage of organisms from the patient to the rebreathing bag of the anesthetizing apparatus, species commonly transferred, and the possibility of disease transmission under supposedly sanitary conditions.

To isolate the more fastidious organisms, samples removed from the apparatus were plated on differential and selective media, and colonies that developed were characterized to determine their pathogenicity. Since patients known to harbor pathogenic bacteria or viruses were not placed under anesthesia in the cases studied,

TABLE 2.—*Bacterial Counts on Apparatus Not Used or Cleaned for Several Days*

Apparatus Tested	Total Bacterial Counts	
	Tube	Rebreathing Bag
B-1	580,000	330,000
B-2	300,000	670,000
B-3	80,000	2,400,000
B-4	250,000	756,000

only a few pathogens of minor significance were anticipated. This should suffice to establish transmissibility.

Anesthetizing apparatus were sanitized immediately following their use by rinsing with tap water and washing with pHisoderm® (a detergent cream composed of a sulfonated ether petroleum, lactic acid, and wool fat cholesterols) containing 3% hexachlorophene. Samples were taken from the tubes and the rebreathing bags, and total counts of microorganisms were determined. Colonies appearing on nutrient agar plates were isolated and studied microscopically, culturally, and biochemically for taxonomic allocation. Contrasting these studies with previous observations should provide insight into the methods of efficient sanitization.

RESULTS AND COMMENT

A study of the sources of several cases of follicular tonsillitis in all patients administered an anesthetic during a one week period indicated the transfer of microbes from patient to patient by inefficiently sanitized apparatus. Further studies by direct counts, isolation, and characterization of microorganisms substantiated previous observations. By taking cognizance of the data in table 1 for apparatus tested immediately after use, it is apparent that organisms pass through the soda lime tower to the rebreathing bag; they should then be capable of being transferred to the next patient anesthetized, since

TABLE 3.—*Bacterial Counts on Apparatus Rinsed with Water Immediately After Use*

Apparatus Tested	Total Bacterial Counts	
	Tube	Rebreathing Bag
C-1	6,300	2,000
C-2	2,460	18,000
C-3	28,000	6,000
C-4	29,000	28,000
C-5	34,600	29,300

one does not pay particular attention to this part of the apparatus. Controls (table 2) show that apparatus that has not been cleaned or used for several days still con-

6. Sulkin, S. E.; Zarafonetis, C., and Goth, A.: Influence of Anesthesia on Experimental Neurotropic Virus Infections: In Vivo Studies with Viruses of Western and Eastern Equine Encephalomyelitis, St. Louis Encephalitis, Poliomyelitis (Lansing), and Rabies, J. Exper. Med. **84**: 277, 1946.

7. Bronfenbrenner, J., and Weiss, H.: Effect of Anesthetics and of Sedatives on Serum Therapy of Experimental Botulism, J. Exper. Med. **39**: 517, 1924.

tains viable organisms (dormant) even though nutrients are absent. Controls in table 3 clearly illustrate that the methods of sanitization employed by hospitals are often inadequate and are therefore conducive to postoperative infections that are usually attributed to other causes.

Particular significance was placed upon the transmission of tuberculosis bacilli, and with this in mind studies were initiated to depict this possibility. Acid-fast Mycobacterium tuberculosis var. hominis and Myco. tuberculosis var. bovis were never shown to be present in apparatus examined; however, patients who were known to harbor tuberculosis bacilli were not anesthetized in any of the cases. Although tuberculosis bacilli were absent, several pathogenic species of microbes were isolated and identified. Pyogenic Micrococcus, Streptococcus, and Pseudomonas aeruginosa were frequently present. These organisms are likely to become secondary invaders and in addition produce serious primary infections in their own right.

Saprophytic micrococci and bacilli were constantly isolated, and even though they are nonpathogenic per se they are occasionally incriminated as secondary invaders complicating more acute diseases. Species of organisms of the genera Bacillus (B. subtilis) and Micrococcus (M. citreus) depict secondary infective agents commonly observed. Viruses were not included in this report although they are certainly transmitted by anesthetizing apparatus. Virus infections would appear to be the most frequently transmitted agents owing to their submicroscopic size and distribution.

Several species of unidentified hemolytic microbes of the genera Micrococcus, Streptococcus, and Bacillus were represented, but their relation or etiology to disease is dubious. These organisms occur with greater frequency in the ether-air tubes than in the rebreathing bags. Aspergillus organisms and one other unidentified organism were obtained in tremendous numbers from the rebreathing bags of some of the apparatus tested. This may be due to the collection of debris in the rebreathing bags, which serves as an excellent pabulum, or to the resistance of the fungal spore. Table 4 will elucidate more emphatically the type of genera and species that have been isolated and identified.

TABLE 4.—*Species of Microorganisms Identified from Anesthetizing Apparatus*

Bacillus species	Aspergillus species
B. subtilis	Alternaria species
B. mycoides	One unidentified genus
Micrococcus species	Pseudomonas species
M. citreus	Ps. aeruginosa
M. pyogenes var. aureus	Flavobacterium species
M. pyogenes var. albus	Sarcina species
Streptococcus species	S. lutea
Str. pyogenes	Candida albicans
Gram-negative bacilli	

Apparatus removed from the patient and immediately sanitized according to routine methods employed (rinsing with tap water) were found to contain viable and dangerous organisms; however, sanitization with water and pHisoderm® with 3% hexachlorophene proved to be an appropriate procedure. This method is suggested for sanitizing anesthetizing tubes and rebreathing bags prior to or immediately after use. Table 5 illustrates the effect of cleansing methods upon the resulting degree of sanitization.

SUMMARY

The passage of microorganisms from the patient to the rebreathing bag of the apparatus used for administering gaseous anesthetics occurs with unrecognized frequency. If the apparatus is not properly sanitized, pathogens may be disseminated to subsequent patients. One must not come to rely upon the removal of microbes by the soda lime tower of the apparatus. These studies demonstrate beyond doubt the passage of microbes from the patient through the tower to the rebreathing bag.

From a preliminary survey of the procedure for administering gaseous anesthetics and the sanitization of used apparatus, it is apparent that more appropriate methods are required. Merely rinsing with water is not sufficient and is not advocated; however, a substantial reduction in the microbial count is obtained by cleansing with pHisoderm® containing 3% hexachlorophene. The pHisoderm® can then be removed by rinsing with water. Frequent cleansing of the rebreathing bag prevents the accumulation of debris, which serves as an excellent medium for the growth of microorganisms. Cognizance should be taken of the data presented in this report, and thus another possible source of disease transmission can be eliminated.

TABLE 5.—*Effect of pHisoderm® Containing 3% Hexachlorophene on the Degree of Sanitization*

Apparatus Tested	Total Bacterial Counts	
	Tube	Rebreathing Bag
D-1	200	200
D-2	1,300	800
D-3	200	100
D-4	500	600

Sir Charles Scott Sherrington (1859-1952).—Running throughout all of Sherrington's work is a broad philosophy to which he seldom referred except by indirection. But it led Leon Asher, when the University of Berne conferred an honorary degree upon Sherrington in 1931, to refer to him as "the philosopher of the nervous system." This brief citation brought a thundering ovation from the huge audience of neurologists, representing virtually every nation of the world, who had gathered at Berne for the first International Neurological Congress. . . . Through the years of his remarkable scientific productivity Sir Charles had continued his interest in poetry, art, and the cultural backgrounds of medicine. It was not widely known that he was an accomplished classical scholar, but perusal of his more recent books, such as "Man on His Nature" and more particularly his "Endeavour of Jean Fernel," will clearly reveal his familiarity with classical texts in which he had always found so much pleasure and relaxation. In preparing for the Fernel, Sir Charles had immersed himself in Galen and the contemporary literature of sixteenth century France. The result is a work of ripe scholarship that would be the envy of any scholar of the period who might have devoted an entire life to the subject. . . . It has been said of him that his genius lay in his extraordinary capacity for translating the facts of morphology into physiological language. This he had done with notable clarity at the spinal and medullary levels; he also elucidated the organization and somatic functions of the cerebral cortex, but he disclaimed any credit for advancing knowledge of mental functions. When discussing the brain as an organ of the mind, Sir Charles insisted, as recently as 1947, that we are no farther along today in accounting for mental processes in physiological terms than was Aristotle two thousand years ago.—J. F. Fulton, M.D., Sir Charles Scott Sherrington, O.M. (1857-1952), *Journal of Neurophysiology*, May, 1952.

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FROSTBITE: AN ANALYSIS OF SEVENTY-ONE CASES

Edward A. Edwards, M.D.
and
Major Roy W. Leeper, United States Army, Boston

Though frostbite is a well-known and serious malady, knowledge of its pathogenesis and of the optimal methods of its management is far from complete. This is due in large part to the paucity of cases coming under the scrutiny of any single group of investigators. The war in Korea in the winter of 1950-1951 resulted in a high incidence of frostbite among our troops. Seventy-one of these patients have been cared for at the Murphy Army Hospital and form the basis for this report. All these soldiers suffered from true freezing of the hands or feet, with resultant necrosis involving at least small areas of deep tissues, and with gangrene of the digits and forepart of the feet in several patients. No cases of cold injury short of this extent are included.

The climatic environment and the combat situation combined to form the epidemiological background of the disease. Most of the patients were frostbitten in north central Korea in the week between Nov. 27 and Dec. 3, 1950. According to information supplied by the Air Force, the temperature in that locality and time reached minimal levels of 12 F. The wind attained a maximal velocity of 20 miles per hour. Our patients were mainly infantrymen. Their protection against the weather was adequate until they were attacked by overwhelming numbers and forced to retreat. The effect of a more stabilized battle line and a more southerly position, which obtained after Dec. 3, served sharply to reduce the incidence of frostbite, though temperatures later dropped as low as −13 F.

The chronology of evacuation is pertinent to the timing of observation and treatment. The time of removal from the field varied from 1 to 11 days after the first onset of symptoms. An aid station was reached in several hours to two days, where the patients usually remained for two to seven days. Further evacuation was by air, the patients arriving at an overseas hospital within a few hours and remaining for about 20 days. Most patients reached the Murphy Hospital three to four weeks after freezing, exceptional cases falling in a range of 17 to 40 days.

We shall describe the clinical picture of the disease, dividing it into acute, subacute, and chronic stages. The acute stage corresponds to the first three or four weeks spent in the overseas medical installations and was characterized by freezing, thawing, exudation, and the initiation of necrosis. Data on this stage were obtained from the patient's history and his medical record. The subacute stage was the one during which the patient was observed at the Murphy Hospital. It was marked by a resolution of the necrosis and the commencement of vasospasm and cutaneous acrosclerosis. From former experience we may expect a chronic stage, consisting of a continuation of the vasospasm and sclerosis, as well as occasional recurrent ulceration.

Data will also be presented bearing on certain unsettled aspects of the frostbite problem, namely, predisposing factors, factors determining severity, the effectiveness of anticoagulant therapy, the recognition of the presence and extent of gangrene, and the late effects of freezing. In 27 patients with severe lesions, special attention was paid to evidence of preexisting cold sensitivity, including examination of the blood for cold agglutinins. The status of the blood vessels was determined, and the Pachon oscillometer was used as an objective check on the examination. The presence and degree of sweating were recorded in several patients through the aid of photography after the ferric chloride and tannic acid reaction.[1] A biopsy of the skin of the extremities was performed in eight patients. Roentgenograms were made of all the involved extremities.

CLINICAL DESCRIPTION

General Data.—The patients numbered 71 and were all men. The majority were 20 to 23 years of age, the range being 18 to 40. In 67 the feet, and in 3 the hands, were the only parts seriously affected. One patient had severe frostbite of both the hands and feet. No instances of freezing of other portions of the body came to our attention. At least superficial necrosis had resulted in all the patients, and gangrene of entire digits in several. Major amputations, comprising those of fingers or of toes and metatarsal heads, were performed in five patients and will be necessary in two more, a total of 10% of all patients. Six more had surgical removal of portions of one or more toes. Finally, in all of the remaining patients, there were at least localized areas of deep necrosis that did not require formal débridement.

At the time of writing of this report 64 patients have recovered, 63 having been sent to duty and 1 discharged for neurosis. Six patients spent 44 to 60 days in the hospital; 50 patients, 61 to 118 days; and 8 patients, 120 to 165 days. Seven patients are still hospitalized.

Predisposition.—The precipitation of the disease in individual cases appeared related either to an exceptional aggravation of the environmental influence or to some predisposition in the soldier himself. Examples of environmental factors noted included removal of gloves or shoes after wounding, accidental wetting of the feet, and exceptional immobility. Three illustrative cases may be cited.

CASE 1.—A 20-year-old infantryman, on the line for several weeks, suffered no ill effects till he received multiple shell fragment wounds of his left forearm and right hand on Nov. 28, 1950. He could now no longer wear his gloves. In the next few days, continuing a retreat on foot, he felt numbness and throb-

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From the Surgical Services, the Peter Bent Brigham and Murphy Army hospitals, and the Department of Anatomy, Harvard Medical School.

Associate in Surgery, the Peter Bent Brigham Hospital, Consultant in Surgery, U. S. Army, and Assistant Clinical Professor of Anatomy, Harvard Medical School (Dr. Edwards); Chief of Section on Dermatology and Syphilology, Murphy Army Hospital (Major Leeper).

1. Silverman, J. J., and Powell, V. E.: A Simple Technic for Outlining the Sweat Pattern, War Med. **7**: 178, 1945.

bing in the hands. On Dec. 2 he suffered a perforating gunshot wound of the middle of the left foot. He crawled through the snow on hands and knees for a few hundred yards, with the hands and left foot exposed. At a first aid station, one-half hour after the second wounding, the hands and feet were observed to be cyanotic, blistered, and swollen. On Dec. 5 he arrived at a hospital, where stellate and lumbar sympathetic blocks were performed; but, despite this, mummification of all the fingers, the left great toe, the ball of the left foot, and the tips of the second, third, and fourth left toes ensued. Only bleb formation and superficial necrosis occurred in the right foot.

Amputation of the fingers and distal part of the thumb of both hands and of the left great toe and metatarsal head was performed on Jan. 25, 1951. Both hands now show residual loss of ulnar blood flow, this being more marked in the left. The pedal pulses are normal, but the feet are cold, sweaty, and cyanotic, and the skin is somewhat rigid.

Fig. 1.—The sweat pattern in the hyperemic and in the vasospastic stages, outlined by ferric chloride and tannic acid. The hands shown are those of the patient in case 3, *A*, 5 weeks, and *B*, 14 weeks, after freezing. In the hyperemic stage the left hand (*A*), more severely frozen, shows none of the sweat reaction. The sweating of the right hand is increased. The left hand has entered on the cold hyperhidrotic stage (*B*), with excessive sweating proximally, but with failure of sweating in the distal, most seriously injured parts. The tapering, shiny appearance of the left fingers is characteristic of the acrosclerosis. Sweating, perhaps in increased amount, is expected to return later in the fingers of the left hand.

Case 2.—This soldier, surrounded by the enemy, hid in caves from Nov. 2 to Nov. 13, 1950. He was well clad but had no gloves. On Nov. 4 he wet his feet in a river. He had no fire for food or warming and did not change his socks. Numbness and pain of the feet resulted. When rescued on Nov. 13, he was found to have redness of the feet, without swelling, and black, dry toes. He reached a hospital Dec. 1, where he received 100 mg. 2-benzyl-2-imidazoline hydrochloride (priscoline*) daily. Bishydroxycoumarin (dicumarol*) was also given from Dec. 6 to Dec. 11. Gangrene of all the toes necessitated bilateral transmetarsal amputations on Dec. 27.

No history of previous sensitivity to cold was elicited. Also, the patient was certain he had not frozen his hands; nevertheless, the hands were cold and cyanotic, and there was moderate pterygium of the fingernails. The feet were similarly cold and cyanotic, to above the ankle on the left and to the middle of the leg on the right. The skin of the feet was rigid and smooth. The peripheral pulses were normal. The patient was comfortable, and it was decided to give him a trial of activity.

Case 3.—An 18-year-old infantryman found himself surrounded by the enemy on Jan. 1, 1951. He was in a foxhole, with his rifle at the ready for 12 continuous hours. In this position the left hand rested on the snow, while the right hand was at the trigger close to the body and lower in the foxhole. In spite of the protection of ski mittens, the left hand became numb and stiff. The next day he reported at a first aid station, where the left hand was found to be white and cold. On the third day it was blistered. On his admission to a hospital Jan. 7 he was given 15 intravenous injections of procaine and nicotinic acid. The blisters formed thimble-like eschars, and the nails blackened. Very slight vesiculation and superficial eschars were found only at the very tips of the fingers of the right hand. The feet were slightly uncomfortable but showed no objective changes.

On examination Feb. 2, it was seen that eschars of both hands had separated. The nails of the left hand, now black, were being shed, and the left hand itself had the characteristics of a "trench foot," being extremely hot, red, swollen, and dry. The right hand was in vasospasm, with marked sweating. The peripheral pulses were normal. Nine weeks later the left hand had become cooler, marked sclerodactyly had developed, and new nails were growing. Sweating had returned everywhere except to the fingertips (fig. 1).

Twenty-seven patients, including those with the most extensive gangrene, were studied with special reference to personal factors that might have predisposed to cold injury. Physical signs taken to indicate the presence of vasospastic disease were coldness, cyanosis, sweating, pterygium of the fingernails (widened cuticles),[2] and rigidity and smoothness of the skin over the digits and the dorsa of the hands and feet. When patients were observed early, and when they could remember the chronic presence of one or more of the signs, a diagnosis was made of the existence of vasospastic disease prior to the frostbite. When signs developed several weeks after freezing, they were interpreted as effects of the cold injury. A history of previous frostbite or trench foot, with residual sensitivity to cold and excessive sweating, was obtained in three patients.

Case 4.—A 25-year-old soldier on Jan. 14, 1951, suffered frostbite of moderate severity in the left foot only. Significant in his history was frostbite of the same foot in January, 1950, while he was a ski trooper with the Army in Alaska. Freezing had been attributed to excessive tightness of a leather strap across the ankle, and he had been hospitalized till July, 1950. Since then the left foot had been cold and sweaty, and painful in cold weather. The patient was exceptional in that he smoked but rarely.

Examination showed an eschar of the left foot and toes that was superficial everywhere except at the very tips of the first and second toes. The foot was cold and sweaty. The right foot and both hands were slightly cool. The pulses were all intact. A left lumbar sympathectomy was performed on Feb. 9, 1951. Progress was satisfactory, and the foot was healed and comfortable by March 30.

Nine patients gave a prior history of coldness, either constant or episodic, and two also had hyperhydrosis. In two additional patients, hyperhydrosis was the only symptom. Cold isoagglutinins were found in only one patient. Whether the presence of isoagglutinins played any part in the frostbite in this person could not be determined. No examination was made for cryoglobulins. No patient gave any history suggestive of cold allergy.

2. Edwards, E. A.: Nail Changes in Functional and Organic Arterial Disease, New England J. Med. **239**: 362, 1948.

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The group of 27 patients was questioned as to their use of tobacco. Twenty were steady smokers of 10 to 30 cigarettes a day. Of the three patients who smoked infrequently, never using more than five cigarettes a day, two had other predispositions to freezing (previous frostbite in one and cold agglutinins in the other), while a third had suffered only minor effects from the frostbite.

Wounding by gunshot or shell fragment seemed clearly to precipitate freezing in six patients. Freezing had either not occurred until the injury or was greatly intensified by it. It must be noted, however, that two of the six patients had suffered from chronic vasospasm and sweating and that a third had suffered from prior frostbite.

CASE 5.—For seven days, ending Dec. 1, 1950, this 23-year-old man was in continuous combat, with no shelter or hot food. The feet were sweaty and soon became numb. On Dec. 1 he received two gunshot wounds, one bullet passing through the superficial tissues about the left knee, the other perforating the right side of the chest, with hemoptysis and subcutaneous emphysema. He was in shock and unconscious during evacuation by truck. At the aid station, on Dec. 2, the feet were found to be "dead white," swollen, and blistered. On Dec. 4, when he reached a hospital, the toes were black and the feet sweaty and cyanotic. His wounds were débrided and the chest closed. Whiskey was given daily.

When seen Jan. 5, 1951, he was observed to have gangrene of the tips of the toes and the distal third of the left great toe. The nails of the right second, third, fourth, and fifth toes had been shed, and the others were dark. The right dorsalis pedis and posterior tibial pulses were of good quality. On the left side the dorsalis pedis could not be felt. There was extreme sweating and coldness of the feet, but the toes did not sweat. A roentgenogram revealed extensive demineralization of the metatarsal heads of the left foot. The hands showed pronounced sweating, coldness, rigidity of skin, and pterygium formation. The patient stated that the coldness, sweating, and enlarged cuticles had been known to him since youth. Paravertebral blocks and intravenous injections of procaine failed to hasten healing or diminish the pain in the left great toe. A left lumbar sympathectomy Jan. 28 resulted in good vasodilatation. After the left great toe was amputated, healing was prompt.

Clinical Course and Management.—1. Acute stage: Data on the initial period of the disease were obtained from the patients and their medical records. The universal immediate symptom was numbness of the affected parts, sometimes preceded by a prickling sensation. Before thawing, the parts were white; after thawing, however, redness, swelling, moderate heat, and a burning sensation were noted. These symptoms were apparently much milder and more transient than those seen in trench foot and usually required no sedation. Blistering, with the formation of large bullae, was also seen within a day or two of thawing. The blisters were at first filled with clear yellow fluid, but this became hemorrhagic within three to five days. A similar process apparently took place between the nail plates and their beds, for hemorrhage occurred beneath many of the nails, giving them a black appearance. Some of these nails were shed within several days, others after a few weeks, as they were pushed forward by a regenerating nail plate. The parts were described as turning black about the fifth day. The blistering and discoloration were distributed over wide zones of the digits and of the hands and feet. The extent of this change bore no relation to the later demarcation of deep necrosis or gangrene (fig. 2).

Thawing of the extremities was ordinarily not possible until the patient arrived at the aid station, because continued freezing often occurred during evacuation from the field. Once the patient was in the aid station, thawing was usually allowed to continue in the room atmosphere. Other treatment consisted only of dressings, tetanus toxoid, and penicillin. Treatment at the overseas hospitals almost invariably included the use of vasodilator substances. About two-thirds of the patients received procaine hydrochloride intravenously in a dose of 1 gm. in 1,000 cc. of isotonic sodium chloride solution, which was repeated daily up to 15 doses. Nicotinic acid, 300 mg. a day, was given alone or with the procaine to about the same number of patients, while priscoline® and whiskey were each used sporadically. Sympathetic nerve block was performed in only four patients. Anticoagulants were used in only two patients, one receiving heparin during the first four days, another bishydroxycoumarin for five days one month after freezing. Both suffered extensive gangrene.

2. Subacute stage: Necrosis was the presenting problem on admission of the patients to the Murphy Hospital in about the third week of the disease. Pain was minimal but was increased when infection was present. A black

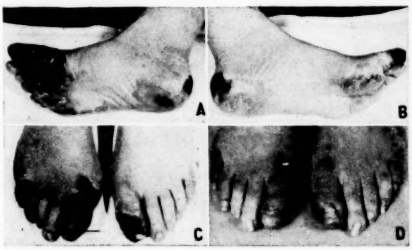

Fig. 2.—Necrosis, resolution, and initiation of acrosclerosis. *A*, *B*, and *C*, three weeks after freezing, show the extent of black eschar. In *D*, 12 weeks after freezing, the slough has separated, disclosing the necrosis to have been superficial. The great toes are, however, shrunken, with tight, rigid skin and regenerating stubby nails. The sclerosis is less pronounced over the other toes and on the dorsa of the feet.

eschar was present over variable portions of the toes and feet, and in three instances over the fingers and hands. In two patients necrosis involved the upper heel, penetrating the insertion of the Achilles tendon. Mummification of gangrenous digits was beginning. Infection was usually minor. The extent of true gangrene could usually not be accurately determined till about the sixth week, since even the superficial portions of the eschar required about four weeks for their separation.

The duration of freezing after the initial symptoms were noted was probably the most significant single factor in determining the severity of tissue damage. When freezing lasted less than one day, the deep necrosis was usually minor in extent; when it lasted two days or more, at least parts of the digits were lost. Patients who were predisposed to freezing in general suffered severer effects than the others. Wounding in the limb or elsewhere was the most significant factor in this regard.

Roentgen studies of the bones proved of limited value. The bones of gangrenous digits revealed no change at all, evidently because of the lack of metabolic exchange (fig. 3). More localized areas of soft tissue necrosis were

occasionally associated with absorption in the underlying bone, with an irregular line of the cortex and a disorganization of the trabeculae, which appeared reticular in arrangement (fig. 4). The typical gross disruption of osteomyelitis was seen beneath badly infected lesions. The atrophy of disuse was seen late, usually about the eighth week of the disease, and it was manifested by a glassy appearance of the metatarsal heads and of the bases of the proximal phalanges (fig. 3).

The occlusion of a peripheral artery was probably indicated by the absence of the dorsalis pedis pulsation on one side, which was noted in 3 patients out of the specially examined group of 27. The lack of pulsation was accompanied by an asymmetry of the oscillometric reading. Only one patient of the three had suffered from previous cold injury.

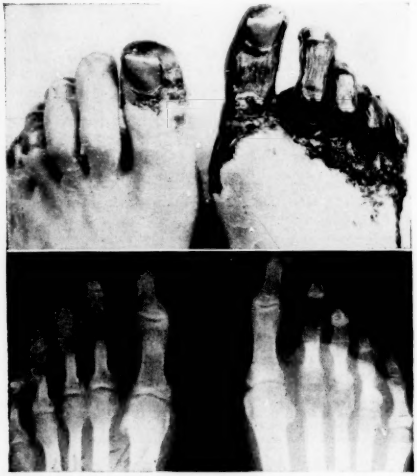

Fig. 3.—Gangrene and the roentgen appearance. This roentgenogram, made eight weeks after freezing, reveals no change either in the gangrenous toes or in the toes showing superficial necrosis. On both sides there is absorption of the heads of the metatarsals and of the bases of the proximal phalanges.

Sympathetic paralysis with hyperemia and dryness of the extremities was seen in a few hands and feet in which the freezing had been only moderate (fig. 1). In some patients with extensive necrosis, a brief hyperemic phase had been noted in the acute stage. Sweating was absent in cold areas from which a fairly deep eschar had separated. In these areas atrophy of the sweat glands may have been important. The absence of sweating, whether or not associated with hyperemia, was often replaced by excessive perspiration as vasospasm supervened.

Vasospasm has already been described, and the point was made that this change often existed in some patients prior to the freezing, while in others the vasospasm was evidently the result of the frostbite, becoming manifest in several weeks. When only one limb had been frozen, the presence of the vessel change in that limb alone supported the contention of its causation by the freezing. Vasospasm was a common effect in the subacute stage, although it was not extreme in degree unless the patient had suffered from prior chronic vasospasm.

Neurological changes consisting of sensory loss were evident in all cases. The loss of sensation was never absolute except over gangrenous parts. It was "glove" or "stocking" in extent, the hypesthesia being most pronounced distally, with normal sensation present at the ankle or wrist. The sensations most affected were light touch and fine temperature discrimination. A light pinprick was often not felt in the most distal parts of the limb, but a stronger pinprick was discernible and pain could be elicited on strong pressure. Deep pressure and vibration sense were not impaired. The neurological findings were consistent with the lack of pain as a complaint during the early weeks of the subacute stage. Pain was felt, however, when active infection was present, and pain was a frequent complaint after the eighth week of the disease, at a time when sensory acuity had returned. The evidence for sympathetic paralysis, and the vascular changes and sweating indicative of sympathetic irritation, have already been discussed.

Cutaneous atrophy and sclerosis were evident over areas where superficial necrosis had been present and to a lesser extent proximally, to the line of the ankle and wrist. The signs of this acrosclerosis became apparent about the sixth week of the disease but certainly progressed somewhat for an additional four weeks. They consisted of shortening of the digits, with thinning of the digital pulp pads; irregularity, thickening, and shortening of the nails; loss of normal wrinkling and surface friction of the skin on the dorsa of the digits, hands, and feet; and rigidity of the subcutaneous tissue (fig. 1 and 2). The changes were those ordinarily described as acrosclerosis. Vasospasm was apparently constantly associated with these changes, but the two processes were not proportional in degree.

A biopsy of the skin was performed in eight patients, specimens being taken from toes or dorsa of the feet, and in two patients of the hands as well. Since the site of biopsy was considerably proximal to the gangrene, the histological examination was more significant as showing the changes of acrosclerosis than as revealing the lesions leading to necrosis. The epidermis was thin, with flattening of the basal papillae. Immediately beneath the epidermis the collagen appeared light, but in the deeper cutis and in the subcutaneous tissue the collagen was heavier than usual. The elastic tissue was fragmented. The sweat glands appeared atrophied in some areas. Small blood vessels showed swelling of the endothelium, and here and there intimal proliferation could be seen. In one patient this process had obliterated the lumen of a small artery. Some nerve fibers showed degeneration with fibroblastic replacement. In general, inflammatory response and fibroblastic proliferation were notably minimal.

Treatment was directed toward the following aspects of the subacute state: (1) prevention and treatment of infection, (2) release of vasospasm, (3) débridement of necrosis, and (4) amputation of gangrenous parts. The affected parts were kept covered with sterile dressings, which were moist if infection was prominent and dry otherwise. Penicillin was used at least initially in all patients. Vasodilating agents (priscoline* or beta-pyridil-

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carbinoltartrate [roniacol®]) were given to those showing much vasospasm. There was no clear-cut evidence that the drugs hastened healing. Lumbar sympathectomy was performed in six patients in whom preexisting vasospasm had been, and still was, severe. This included the three persons in whom one dorsalis pedis pulse was missing. Sympathectomy was distinctly helpful in speeding healing as well as in giving a warm, comfortable limb.

Removal of the superficial eschar was aided by cutting away loosened portions in order to allow an earlier delineation of the extent of the deep necrosis. Deep necrotic tissue was likewise removed from time to time as demarcation became evident, exposed portions of bone being rongeured back. Amputations, when necessary, were performed close to the line of demarcation, with satisfactory healing.

3. Chronic stage: The changes we know to be characteristic of the chronic stage of frostbite could already be observed in most of our patients during their hospital stay. The sclerodactyly noted several weeks after freezing often increased as healing took place. The affected digits thus became shortened, with atrophy of the digital pad, with an irregular nail plate, and with the smooth, rigid skin of the digit and hand or foot already described (fig. 1 and 2). Vasospasm and hyperhidrosis gradually disappeared in some limbs but remained prominent in others, especially where cold sensitivity had existed prior to freezing. Pain was now a more frequent complaint, not only in the scars resulting from the necrosis but also in the more proximal parts.

COMMENT

Etiology.—Stated in simplest terms, an extremity is frozen when its loss of heat is greater than can be offset by local heat production or by local warming from the blood perfusing the limb. As regards heat loss, both the temperature of the ambient air and the wind velocity are important. Humidity is so low at freezing temperatures as to be of negligible importance. Wetting of the foot gear, either by perspiration or by accidental immersion, greatly increases the tendency to freezing, since water transfers heat 23 times more readily than air.

The effective blood perfusion of the limbs is diminished via peripheral vasoconstriction from a variety of causes incident to adverse combat conditions. Even with so-called adequate clothing, a man exposed to severe winter weather often suffers considerable chilling and peripheral vasoconstriction. Under ordinary circumstances this chilling is not allowed to continued uninterrupted for many hours, being relieved by the general warming and vasodilatation occasioned by eating, especially when the food is hot, and by intermittent shelter and warming, especially during sleep. When this relief from chilling is denied, vasoconstriction is unrelieved. Hunger, exhaustion, and anxiety all increase the vasoconstriction. The vasoconstrictive effects of tobacco smoking may aid in this process and help to induce freezing. Wounding appears to be an effective precipitant of freezing, adding the vasoconstriction of shock and hemorrhage, loss of blood volume, wetting of the part with blood, and bodily immobility. Blair states that 35% of all cold injury patients seen in the army had been wounded prior to the development of the frostbite.[3]

It is widely known, in a general way, that persons vary in their response to cold. We have noted more specifically that many of our patients had suffered from chronic vasospasm and that a few had suffered previous freezing or trench foot. It would seem that soldiers showing stigmas of cold sensitivity, or with a history of previous cold injury, are poor subjects for duty in freezing climates. Further search seems indicated for evidence, in cold injury patients, of the presence of isoagglutinins (cold agglutinins) and cryoglobulins. The role of a low basal metabolism might also be investigated with profit, since it is known that the temperature of the extremities

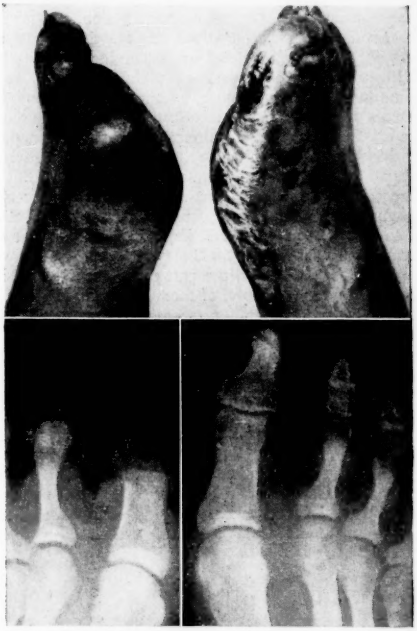

Fig. 4.—Roentgen findings associated with superficial necrosis. The film, made nine weeks after freezing, shows on the right, spotty absorption with disruption of the trabeculae in the head of the metatarsal and in the head of the first phalanx of the great toe (corresponding to the area of maximal injury seen in the photograph). The necrosis of the stump of the previously amputated left great toe was not accompanied by any roentgen change.

in patients with a low metabolic rate drops lower under adverse conditions, such as tobacco smoking, than does that of patients with a higher rate.[4]

Pathogenesis and Treatment.—A brief statement of the mechanisms responsible for the effects of frostbite will suggest the rationale of treatment. Two excellent reviews [5] may be consulted for the present status of our knowledge in this field. It appears that necrosis may be

3. Vascular Surgery: Cold Injuries, National Research Council, 64-126, 1951.

4. Roth, G. M.: Tobacco and the Cardiovascular System, Springfield, Charles C Thomas, Publisher, 1951.

5. (*a*) Footnote 3. (*b*) Kreyberg, L.: Development of Acute Tissue Damage due to Cold, Physiol. Rev. **29**: 156, 1949.

caused by one or more of the following factors: (1) direct injury from the freezing itself, with evidence most striking in the case of muscle [3] and nerve tissue,[6] (2) edema of the hyperemic phase, which ensues soon after thawing,[7] and (3) vascular occlusion by "conglutination" of the blood cells in the vessels in the early hours after thawing, or by larger thrombi in which some fibrin is seen and which develop some days after thawing.[8]

Anoxia due to lack of dissociation of oxygen from hemoglobin at low temperatures is probably unimportant in the actually frozen tissue, since its metabolism is adequately depressed. Changes in the blood vessels themselves, consisting of early swelling and vacuolization of the intima, with later changes of proliferation, are known to occur early and to continue into the chronic stage. These changes are probably not responsible for the early necrosis but may cause some of the chronic effects.[9] The duration of exposure, once freezing has commenced, seems of extreme importance in the extent of the subsequent gangrene of the entire part. This was true in the experience of Brahdy,[10] as well as in our present study. Rapid thawing is thought by many to significantly reduce the effects of frostbite.[3] Rapid thawing, as defined by Schumacker and Lempke,[3] consists of immersion of the frozen parts in water at 42 C. They agree with others that temperatures as high as 50 C may be harmful and urge also that, once thawed, the part should be allowed to remain at the cooler level of room temperature. Rosenfeld and his co-workers [11] present the contrary view that rapid thawing increases the necrosis, at least after experimental freezing in the dog. Attempts to diminish the effect of the edema by the use of pressure bandages or casts have not altered the course of the disease. Experimentally edema is increased by early sympathectomy or post-thawing heating, with increase in pain and perhaps in necrosis.[5]

The importance of blood cell stasis and thrombosis in producing ischemia and subsequent necrosis was emphasized by students of the frostbite problem in World War II, notably Greene [8b] and Friedman.[8c] Lange and Boyd [12] utilized visualization by fluorescein to demonstrate that maximal hyperemia of the frozen tissues at 4 hours after thawing is followed by a lack of circulatory exchange at 48 hours. These authors suggested the use of heparin to prevent the red blood cell conglutination responsible for the circulatory stasis. Kreyberg [5b] sums up the considerable evidence that heparin does not prevent the early conglutination. Friedman, Lange, and Weiner [13] have come to agree with this view, but nevertheless hold that heparin will prevent the formation of secondary agglutinative thrombi and is therefore important in preventing necrosis. This group emphasizes that the heparin must be given early and in adequate dosage to prolong the coagulation time uninterruptedly for at least five days after freezing.[14] The available reports on treatment of human cases with anticoagulants seem inconclusive. A further, well-controlled clinical trial with this mode of therapy would appear highly desirable.

Our data support the view that the release of sympathetic tone by medical or surgical means is not useful in the acute stage of frostbite. Indeed, experimental work previously available [15] had suggested that vasodilatation may be harmful at that time. It is in the subacute and chronic stages of the disease, when vasoconstriction is prominent, that release of sympathetic tone would seem effective. Surgical sympathectomy in the subacute stage is particularly desirable when it appears reasonably certain that chronic sequelae would otherwise result. At the present we are unable to predict accurately the future course of the disease in all patients. As a working rule we propose that loss of a major peripheral pulse, or severe chronic vasospasm existing prior to the frostbite, be considered indications for the operation. Indications in the chronic stage include recurrent ulceration or pronounced vasospasm and discomfort that have failed to disappear after the freezing. Judging by experience with veterans of World War II, it would seem that a period of about two years might be considered adequate time for such symptoms to clear spontaneously.

SUMMARY AND CONCLUSIONS

The clinical course of 71 cases of frostbite of the extremities, all showing necrosis, is described. The patients were all soldiers, and the precipitating factor was the adverse combat situation. Personal factors of importance in the causation of the freezing were the existence of chronic vasospasm or hyperhidrosis, previous cold injury, wounding, and possibly tobacco smoking.

The disease is described in three stages: (1) the acute, characterized by the freezing, thawing, blistering, and beginning of necrosis; (2) the subacute, during which the necrosis is resolved and vasospasm and acrosclerosis start; and (3) the chronic, when the vasospasm and acrosclerosis continue and pain and recurrent ulceration may occur. Treatment during the acute stage consisted mainly of administration of antibiotics and sympathicolytic drugs. Anticoagulants were used in only two patients. In the subacute stage use of antibiotics and sympathicolytic drugs was continued, and the eschar was gradually removed. Sympathectomy was done in six patients in whom preexisting vasospasm had been pronounced.

6. Denny-Brown, D.; Adams, R. D.; Brenner, C., and Doherty, M. M.: The Pathology of Injury to Nerve Induced by Cold, J. Neuropath. & Exper. Neurol. **4**: 305, 1945.

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8. (*a*) Kreyberg,[5b] (*b*) Greene, R.: The Immediate Vascular Changes in True Frostbite, J. Path. & Bact. **55**: 259, 1943. (*c*) Friedman, N. B.: Reactions of Tissue to Cold: Pathology of Frostbite, High Altitude Frostbite, Trench Foot and Immersion Foot, Am. J. Clin. Path. **16**: 634, 1946.

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10. Brahdy, L.: Frost-bites Among Employees of the City of New York During the Winter of 1933-1934, J. A. M. A. **104**: 529 (Feb. 16) 1935.

11. Rosenfeld, L.; Langohr, J. L.; Owen, C. R., and Cope, O.: Circulation of the Blood and Lymph in Frostbite and Influence of Therapeutic Cold and Warmth: Experimental Study, Arch. Surg. **59**: 1045, 1949.

12. Lange, K., and Boyd, L. J.: The Functional Pathology of Experimental Frosbite and the Prevention of Subsequent Gangrene, Surg., Gynec. & Obst. **80**: 346, 1945.

13. Friedman, N. B.; Lange, K., and Weiner, D.: The Pathology of Experimental Frostbite, Am. J. M. Sc. **213**: 61, 1947.

14. Lange, K.; Boyd, L. J., and Weiner, D.: Prerequisites of Successful Heparinization to Prevent Gangrene After Frostbite, Proc. Soc. Exper. Biol. & Med. **74**: 1, 1950.

15. Kreyberg,[5b] Arena, J. A., Jr.; Gerbasi, F. S., and Blain, A., III: Experimental Frostbite: An Inquiry into the Effect of Sympathetic Block Using Tetra-ethyl Ammonium Chloride in the Acute Stage, Angiology **1**: 492, 1950.

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The superficial necrosis was always more extensive than any underlying gangrene, and observation over several weeks was necessary before amputation was performed. Amputations of fingers or of toes at metatarsal levels were necessary in seven patients, while amputations of portions of toes were necessary in six additional patients.

The duration of freezing after initial symptoms was the most important single factor in the extent of necrosis. Patients showing personal predisposition to freezing, especially those wounded, also suffered most severely. The use of sympathicolytic drugs in the acute stage seemed to have no effect on the outcome. Anticoagulants would appear to deserve a more thorough trial, and more data may help in the question of rapid versus slow thawing.

Sympathectomy appeared to hasten healing in the patients operated on in the subacute stage. It would seem to be indicated when severe vasospasm or other vascular disease has existed prior to the freezing or when the frostbite has caused loss of a peripheral pulse. It is not possible to predict accurately which patients will show long-lasting chronic effects. It is suggested that one wait no longer than two years for spontaneous disappearance of symptoms before performing sympathectomy.

330 Dartmouth St. (Dr. Edwards).

METASTASIS OF RECTAL CARCINOID TO THE BROAD LIGAMENT

C. H. Epps, M.D., R. N. White, M.D.
and
E. B. Hanan, M.D., Springfield, Mo.

It is our purpose in reporting this case to call attention to an extremely uncommon tumor of the broad ligament. The tumor in our case proved very confusing as to identity until it was found to be metastatic from a small inconspicuous primary lesion of the rectum.

The adnexae and parametria have been the site of many unusual tumors. Many of these tumors have been difficult to identify as evidenced by the numerous suggested classifications of ovarian tumors. The development of these structures gives rise to innumerable possibilities for different types of tumors and for their appearance in unusual locations. Reports of carcinoids in this region, however, are rare. Stewart and Taylor [1] described a patient with primary carcinoid of the appendix with two metastatic nodules implanted on the pelvic peritoneum; the patient was well 10 years after the removal of the appendix and the two nodules from the cul de sac. Siburg [2] reported a case of carcinoid of the rectum with extensive metastases to sacral and aortic lymph nodes, vertebra, liver, and chest with a rapidly fatal course. Stewart, Willis, and de Saram [3] described two patients with dermoid cysts of the ovary with areas of argentaffin carcinoma, one of whom was well three and one-half years after surgery. We have been unable to find any reported case of carcinoid that resembled an intraligamentary tumor or any case of carcinoid of the rectum with metastasis to this region. We believe that ours is the first reported case of carcinoid of the rectum metastasizing to the broad ligament and also the first reported case of carcinoid of the rectum with known metastasis of four years' duration. Our case is also unusual in that the metastatic tumor was found before the primary tumor in the rectum was discovered, which gave rise to considerable speculation and discussion as to its classification and origin.

As early as 1888 Lubarsch [4] reported two cases of multiple small submucosal cancers of the small bowel composed of nests of uniform cells not resembling cells of the intestinal mucosa, and in 1901 Whipham [5] reported unusual yellow carcinomas of the ileoceal region and referred to 18 cases reported by Kelly, one by Rolleston, and one by Hurdons. Whipham's description of the histological changes was remarkably similar to descriptions by present day authorities, but it was not until 1907 that Oberndorfer,[6] who believed them to originate from the mucosa and to be benign, suggested the term "carcinoid." Saltykow [7] probably reported the first carcinoid of the rectum in 1912. Numerous investigators have objected strenuously to the term carcinoid and have proposed such terms as "argentaffinomas,"[7a] "Kultschitsky cell tumor," and "carcinoma grade 1 (Broders [7b])," but the term carcinoid still prevails. Since Horn and other authorities have demonstrated that not all rectal carcinoids contain argentaffin granules and that some rectal carcinoids contain mucin, it seems that the term carcinoid is probably as good as any, particularly since the malignant potentiality is well recognized but extremely variable.

There are excellent reviews of the literature pertaining to carcinoids of the rectum by Horn,[8] Stout,[9] Pearson

From the Departments of Surgery, Obstetrics, and Pathology, Burge Hospital.

1. Stewart, M. J., and Taylor, A. L.: Carcinoid Tumor of the Appendix with Large Pelvic Deposits, J. Path. & Bact. **29**: 136-139, 1926.

2. Siburg, F.: Über einen Fall von sogenanntem Karzinoid des Rektums mit ausgedehnter Metastasenbildung, Ztschr. f. Path. **37**: 254-269, 1929.

3. Stewart, M. J.; Willis, R. A., and de Saram, G. S. W.: Argentaffine Carcinoma (Carcinoid Tumour) Arising in Ovarian Teratomas, J. Path. & Bact. **49**: 207-212, 1939.

4. Lubarsch, O.: Ueber den primären Krebs des Ileum nebst Bemerkungen über das gleichzeitige Vorkommen von Krebs und Tuberculose, Arch. f. path. Anat. **111**: 280-317, 1888.

5. Whipham, T. R. C.: A Case of Primary Carcinoma of the Vermiform Appendix, Lancet **1**: 319-321, 1901.

6. Oberndorfer, S.: Karzinoide Tumoren des Dünndarms, Ztschr. f. Path. **1**: 426-432, 1907.

7. Saltykow, S.: Ueber die Genese der "karzinoiden Tumoren," sowie der "Adenomyome" des Darmes, Beitr. z. path. Anat. u. z. allg. Path. **54**: 559-594, 1912.

7a. Willis, R. A.: Argentaffin Carcinomata ("Carcinoids") of the Small Intestine, M. J. Australia **2**: 400-403, 1940.

7b. Dockerty, M. B., and Ashburn, F. S.: Carcinoid Tumors (So-Called) of the Ileum: Report of Thirteen Cases in Which There Was Metastasis, Arch. Surg. **47**: 221-246 (Sept.) 1943.

8. Horn, R. C., Jr.: Carcinoid Tumors of The Colon and Rectum, Cancer **2**: 819-837, 1949.

9. Stout, A. P.: Carcinoid Tumors of the Rectum Derived from Erspamer's Pre-enterochrome Cells, Am. J. Path. **18**: 993-1009, 1942.

and Fitzgerald,[10] and Pautler and Scotti.[11] Horn's report probably is the most recent and comprehensive; he reports 56 cases, including six of his own. Of the 56 lesions, five were malignant. Since Horn's report, Shepard and co-workers [12] reported two cases of carcinoid of the rectum, both of which were locally invasive but without

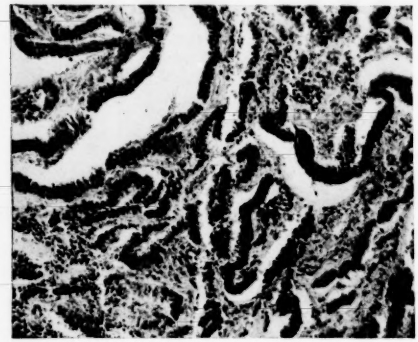

Fig. 1.—Metastatic tumor of broad ligament (× 170).

metastasis. Wilson [13] reported another small carcinoid in the rectum, but in his case there was one metastatic gland at the upper end of the rectum in the mesentery. Early in 1951 Hines and Riddler [14] reported three cases of rectal carcinoids with no mention of metastases, and Mayo and McKee [15] reported two cases of polypoid carcinoids with no known metastases. Seven other cases were mentioned in a paper by Pearson and Fitzgerald,[10b] which were observed at the Memorial Hospital in New York, but no details were given as to location, age, or malignancy. The addition of our case makes a total of 72 cases of rectal carcinoids, in seven of which the lesion was definitely malignant. Some evidence as to the rarity of rectal carcinoids is gained by the fact that Stout [9] found only two cases in 13,809 routine autopsies and Hines and Riddler [14] found only three cases in 30,000 routine proctological examinations.

In spite of the malignant tendency of some carcinoid tumors, several reports show that metastases may lie dormant for several years. Terplan [16] reported a carcinoid of the cecum with metastases in mesenteric glands and liver, in which a biopsy and palliative ileocolostomy was done. The patient died by drowning three and a half years later, and the autopsy showed no progression of the tumor or metastases. Merke [17] reported a case in which a palliative ileocolostomy was done; the patient died of pneumonia and erysipelas five years later, and the autopsy showed no progression of the tumor. Decker [18] reported another case in which carcinoid tumor was found in mesenteric glands, but at autopsy, two and a half years later, no tumor could be found. Mallory [19] reported a most unusual case in which a segment of ileum was resected for carcinoid, with known mesenteric metastases left behind. The patient died 20 years later of pneumonia, and the autopsy showed no further extension of the tumor. Horn's [8] patient with carcinoid of the rectum with extensive metastases lived 17 months, but in this case death was due to metastatic disease.

Another unusual feature we observed in studying the literature was the relatively high incidence of these tumors on the anterior rectal wall, 5 to 10 cm. from the anal margin. In our case the lesion was typically situated on the anterior wall, about 6 to 8 cm. from the anal margin. Of the 72 cases reported in the literature, 22 were of lesions located on the rectal wall. In 14 (an incidence of 64% if the same ratio holds for all of the other cases) the primary tumor was located on the anterior rectal wall, in 3 on the posterior wall, and in 2 on the lateral wall. In two cases the lesion was annular and in one case it was diffuse. In the remaining 50 cases the site was not specified.

REPORT OF A CASE

Mrs. M. T., a 26-year-old white woman, was first admitted to Burge Hospital Oct. 18, 1950, complaining of dyspareunia and a tumor of the left ovary. She stated that the tumor was first found on postpartum examination, in September, 1946,

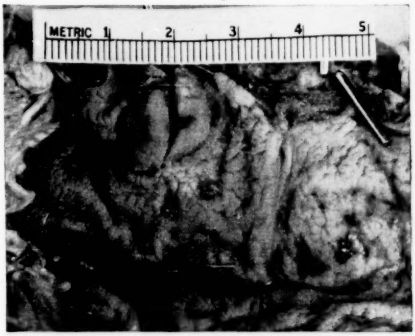

Fig. 2.—Gross Appearance of the primary tumor of the rectum. (The location in the rectum is distorted because the specimen was fixed before it was photographed.)

after the birth of her first baby, and that no treatment was advised. She was first seen by one of us (R. N. W.) in October, 1947; she had a normal pregnancy, but the tumor of the pelvis was not noted at the time. She had a normal delivery in April, 1948. On June 23, pelvic examination revealed what was thought to be a prolapsed left ovary. She was examined fairly frequently after this, and in October, 1948, the ovary was thought to be larger. In September, 1949, she again returned, complaining of

10. (*a*) Pearson, C. M., and Fitzgerald, P. J.: Carcinoid Tumors of the Rectum: Report of Three Cases, Two with Metastases, Ann. Surg. **128**: 128-143, 1948; (*b*) Carcinoid Tumors—Re-emphasis of Their Malignant Nature: Review of 140 Cases, Cancer **2**: 1005-1026, 1949.

11. Pautler, E. C., and Scotti, T. M.: Carcinoid in Meckels' Diverticulum: Report of a Case and Review of the Literature Including Usual and Unusual Sites of Carcinoids, Gastroenterology **17**: 88-95, 1951.

12. Shepard, R. M., Jr.; Strug, L. H., and DiLeo, J. H.: Carcinoid Tumors of the Rectum, Surgery **29**: 205-209, 1951.

13. Wilson, H.: Carcinoid of the Rectum, Arch. Path. **48**: 187-189 (Aug.) 1949.

14. Hines, M. O., and Riddler, J. G.: Unusual Lesions of the Rectum and Anus, Surgery **29**: 496-499, 1951.

15. Mayo, H. W., Jr., and McKee, E. E.: Carcinoid of the Rectum, A. M. A. Arch. Surg. **62**: 506-513 (April) 1951.

16. Terplan, K.; Weintraub, D., and Wolf, N. J.: Stationary Metastasizing Carcinoid of the Ileocecal Valve, Arch. Path. **30**: 1155 (Nov.) 1940.

17. Merke, F.: Das Karzinoid der untersten Ileumschlinge, Schweiz. Med. Wchnschr. **67**: 639-641, 1937.

18. Decker, P.: Contribution a l'étude du carcinoïde, Rev. méd. de la Suisse Rom. **48**: 145-146, 1928.

19. Case Records of the Massachusetts General Hospital: Case 26162 [Carcinoid of the Ileum], New England J. Med. **222**: 684-687, 1940.

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low backache and rectal bleeding. An examination at this time revealed the same firm mass in the region of the left ovary, but at this time it was definitely thought to be a tumor in the broad ligament. She was seen in consultation by one of us (C. H. E.); and the diagnosis of an intraligamentary solid tumor was confirmed. A sigmoidoscopic examination disclosed nothing essentially abnormal except for bleeding hemorrhoids. The patient

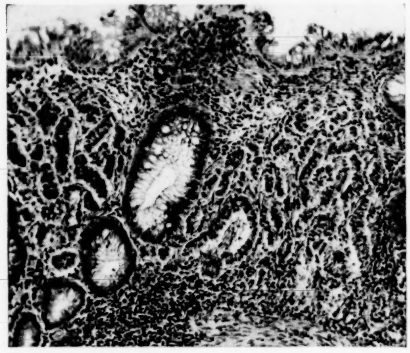

Fig. 3.—Primary rectal carcinoid (× 95).

was advised to have the tumor removed at this time, but she declined to do so and she was not seen again until September, 1950, when she returned complaining of dyspareunia, low backache, and rectal bleeding and requested surgery.

Her physical examination disclosed nothing abnormal except in the rectum and pelvis. Pelvic examination revealed a parous introitus with fairly good support. The cervix was lacerated bilaterally and mildly eroded, and the uterus was anterior and normal. The right adnexa was normal; but on the left a firm and tender mass, the size of an English walnut, was found deep in the broad ligament just to the left of the cervix. The ovary was palpable anterior to this mass. Rectal examination revealed moderate internal and external hemorrhoids, which bled from the trauma of the anoscope. Laboratory findings were all within normal limits, and the Kahn reaction was negative.

On Oct. 19, pelvic laparotomy was performed. A tumor, approximately 4 by 4 by 5 cm., was found at base of left broad ligament. The peritoneum over the tumor was incised, and the nodule was shelled out easily. Hemostasis was secured and the peritoneum closed. The remainder of the abdomen was explored and found to be entirely normal. The appendix was removed, and the abdomen was closed in the usual manner. The postoperative course was uneventful.

The tumor nodule was studied by one of us (E. B. H.) and thought to be of unusual origin and probably of low-grade malignancy. Dr. Lauren Ackerman (Washington University School of Medicine, St. Louis), who studied the microscopic preparations, felt the tumor was of low-grade malignancy and probably metastatic from the large bowel. Sections of the tumor were sent to several other national authorities, most of whom agreed that it was of low-grade malignancy. Because of its location in the broad ligament, one authority felt it arose from remnants of the wolffian duct; another suggested its origin from the müllerian duct; and another thought it to be a granulosa cell tumor of the ovary. Still another thought it to be a benign tumor arising from remnants of the müllerian duct. On Dr. Ackerman's suggestion a thorough examination was made, which revealed a small tumor on the anterior rectal wall 6 by 8 cm. above the anal margin. A biopsy of this nodule was interpreted as adenocarcinoma.

On Dec. 2, an abdominoperineal resection was done; a portion of the left hypogastric vessels and some of the remaining scar tissue, where the metastasis had previously been removed, were excised. The patient had an uneventful convalescence following this last procedure. The pathologist found the primary tumor to be essentially submucosal, with some muscle infiltration but confined to the bowel wall. In the adjacent lymph nodes and tissue removed from the pelvic wall he found no tumor cells. The final diagnosis was carcinoid of the rectum with retroperitoneal metastasis. Because tumor tissue might have been left on the left pelvic wall, the patient was given a course of roentgen therapy; she was discharged in good condition. During the period Jan. 3 to Feb. 1, 1951, a total of 2,200 r (air) was delivered to each of four anterior and posterior pelvic ports, measuring 10 by 12 cm. each, with the following factors: 250 kv., Thoraeus II filter, and half-value layer of 2.32 mm. copper.

Pathological study of the metastatic tumor revealed it to be firm, 4 by 4 by 5 cm., and well circumscribed, with a slightly bosselated surface. The cut surface revealed a slightly bulging homogenous pale yellowish pink surface with small focal hemorrhages. Microscopic sections showed it to be composed of numerous strands and cords of regular low columnar and cuboidal cells with uniform even-staining nuclei. In most areas the strands were made up of double rows of cells with characteristic festooning as described by Stout (fig. 1).

The second specimen consisted of sigmoid and rectum 30 cm. in length and several small pieces of fibrous tissue. The surface of the colon, rectum, and anal skin all appeared normal, and a careful search of the mesentery failed to reveal any enlarged lymph nodes. When the specimen was opened, the mucous membrane appeared normal except for a 1 by 1 by 1.5 cm. firm elevated nodule on the anterior wall of the rectum 8 cm. above the anal orifice, with no gross evidence of ulceration. The cut surface showed the same firm homogenous white tissue as noted in the metastatic tissue and apparently was limited to the submucosa. The gross appearance is shown in figure 2. Microscopically the tumor was situated in the submucosal layer, pushing the epithelium upward and thinning it out in its center and in small areas producing ulceration. The base of the tumor invaded the muscle superficially but did not extend through the wall. The same cell pattern and architecture as observed in the metastatic tumor were noted. Sections of the rectal tumor are shown in figures 3 and 4.

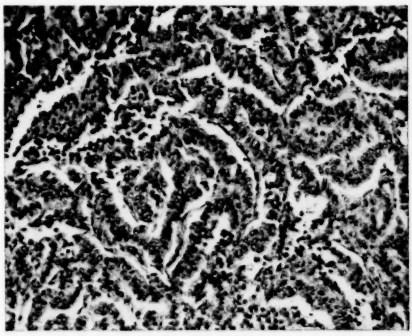

Fig. 4.—Primary rectal carcinoid (× 125).

COMMENT

The pathological changes of rectal carcinoids have been thoroughly studied and adequately described. The carcinoids are characteristically small, firm, hemispherical submucosal nodules situated frequently on the anterior rectal wall 3 to 10 cm. above the anus (table 1). Although Rigdon [20] reported a case in which the entire rectum was covered with small nodules, Pearson and

20. Rigdon, R. H., and Fletcher, D. E.: Multiple Argentaffin Tumors (Carcinoids) of the Rectum, Am. J. Surg. **71**: 822-824, 1946.

Fitzgerald [10] reported a large annular lesion, and Koch [21] reported a similar constricting lesion, the primary tumor is usually small and single. The benignity of metastases in some instances is exemplified in Horn's patient, with 17 months' survival in the face of extensive spread, and in our own patient, with metastasis of four years' duration and no evidence of spread to other organs or nodes.

All authorities are agreed that these tumors arise from the Kultschitzky (basigranular) cells at the base of the crypts of Lieberkühn. Stout refined this further by suggesting their origin from the pre-enterochrome cells of Erspamer, thereby explaining the absence of argentaffin granules in most of these tumors. Erspamer divided the basigranular (Kultschitzky) cells into four groups, of which the pre-enterochrome cells represent an earlier stage of development and do not show an affinity for

TABLE 1.—*Previously Reported Cases of Carcinoid of the Rectum*

Author	No. of Cases	Date	Age of Patient	Sex	Location in Rectum and Size (When Recorded)	Metastases	Treatment and/or Remarks
Saltykow [7]	1	1912	28	F	Anterior wall; 5 cm. above anus	None	Puerperal death; incidental autopsy finding
Staemmler *	1	1924	35	F	10 cm. above anus	None	
Martin and Dechaume †	1	1924	56	M	.....	None	Incidental findings with surgical tissue
Silburg [2]	1	1929	71	M	Anterior wall, 4 cm. above anus	Lymph nodes (sacral, aortic), vertebra, liver	Exploratory laparotomy; autopsy later
Brunschwig [23b]	1	1933	63	M	Anterior rectal wall, 8 cm. above rectum	None	Local excision
Feyrter ‡	5	1934	14	M			
			54	F			
			56	F			
			59	F			
			67	F			
Koch [21]	1	1940	64	M	2-3 cm. above anus; infiltrative lesion constricting 10 cm. of rectum to pencil size	Lymph nodes, liver, bladder, ureters	Autopsy finding
Humphreys §	1	1934	28	M	.....	Apparently none	Autopsy finding
Mallory [19]	1	1940	?	?			
Ashworth and Wallace ‖	1	1941	31	F	10 cm. within rectum; wall not mentioned	None	Abdominal perineal resection
Stout [9]	6	1942	19	F	Anterior wall; 2 cm. mass	.....	Local removal
			41	F	Anterior wall; 5 cm. mass	.....	Local removal
			34	F	Anterior wall; 1 cm. mass	None	Local removal
			34	F	Anterior wall; 5 cm. mass	.....	Local removal
			42	F	Anterior wall; 7 cm. mass	.....	Autopsy finding (mediastinitis)
			43	M	Just above anus	.....	Autopsy finding (stomach operation)
Helwig [23c]	1	1943	56	M	?	None	Local (?) excision
Yaker [23c]	1	1944	29	M	Anterior wall; ½ in. tumor 4 in. within rectum	None	Local excision
Rigdon and Fletcher [20]	1	1946	60	M	15 cm. of rectum covered with argentaffin nodules	None	Ruptured aneurysm Incidental autopsy findings
Severance ¶	1	1946	33	F	?	None	Routine examination for vaginal bleeding
Dukes [23d]	9	1946	(5 no age given)			Apparently none in any of 9	Incidental findings in 3 in surgical specimen; no follow-up
			40	F	Lower ⅓ of wall?		Local excision
			34	F	Same		Local excision
			36	F	?		Local excision
			36	M	?		Local excision; well 9 yr.
Wilson [13]	1	1949	57	F	.....	One node at upper end of resection	Abdominal perineal resection
Shepard [12]	2	1950	61	F	Anterolateral wall	None	Abdominal perineal resection
			54	M	Posterior wall, 6 cm. up	None	Abdominal perineal resection
Jackman ‡	4	1947	?	?	?	None apparently	Apparently local excision in all
Ehrlich and Hunter **	10	1947	?	?	?	None	All excised locally
Pearson and Fitzgerald [10a]	3	1948	51	M	3 tumors in posterior and anterior wall	Liver, kidney	Exploratory laparotomy; autopsy later
			45	F	Annular lesion	Liver, aortic nodes	Exploratory laparotomy; palliative colostomy
			69	M	Left anterior wall at rectosigmoid junction	None	Local excision
Horn [8]	6	1949	29	F	Right lateral wall, 1 cm. above anus	Adrenals, pancreas, liver, lungs, spleen	Autopsy (death from liver disease)
			42	F	?	None	Local excision
			56	F	?	None	Local excision
			25	F	?	None	Local excision
			..	M	?	None	Local excision
			62	M	?	None	Local excision
Hines and Riddler [14]	3	1951	49	..	Anterior wall, 4 cm. up; 3 cm. nodule	.....	Local excision
Mayo and McKee [15]	2	1951	24	F	Polyp, 1 cm., at 6 cm. level	Right lateral wall	
			29	M	Polyp, 1 cm., at 5 cm. level	Right posterior lateral wall	

* Staemmler, M.: Das sogenannte Karzinoid des Darmes, Neue deut. Chir. **33a:** 230-244, 1924.
† Martin, J. F., and Dechaume, J.: Double adénome endocrinien du rectum, Lyon méd. **133:** 686-688, 1924.
‡ Feyrter, F.: Carcinoid und Carcinom, Ergebn. d. allg. Path. u. path. Anat. **29:** 305-489, 1934.
§ Humphreys, E. M.: Carcinoid Tumors of the Small Intestine: A Report of Three Cases with Metastases, Am. J. Cancer **22:** 765-775, 1934.
‖ Ashworth, C. T., and Wallace, S. A.: Unusual Locations of Carcinoid Tumors, Arch. Path. **32:** 272-276 (Aug.) 1941.
¶ In Stout, A. P.: Tumor Seminar: Carcinoid Tumor of the Rectum (Case 1), Texas State J. Med. **41:** 564, 1946.
‡ Jackman, R. J.: Submucosal Nodules of the Rectum: Diagnostic Significance, Proc. Staff Meet., Mayo Clin. **22:** 502-504, 1947.
** Ehrlich, J. C., and Hunter, O. B., Jr.: Tumors of the Gastrointestinal Tract: A Survey of 813 in Persons of Military Age During World War II, Surg., Gynec. & Obst. **85:** 98-106, 1947.

21. Koch, F.: Maligne Carcinoide, Chirurg **12:** 270-275, 1940.

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silver stains. All of the reported cases of rectal carcinoids are shown in table 1. Table 2 shows the relative frequency of carcinoids of the rectum as compared to carcinoids occurring in other unusual locations. Most of the patients described were older than our patient; all the patients with malignant carcinoids were older.

Most authors [22] consider rectal carcinoids, as well as carcinoids in other portions of the bowel, as definitely malignant but slow growing and slow to metastasize. Ackerman [22b] believes the infrequency of metastases in carcinoids of the appendix and rectum is based on the fact that they give rise to symptoms early. In the case of appendiceal carcinoids, the symptoms are obstructive and usually appendectomy is performed before metastases take place. In rectal cases bleeding, tenesmus, diarrhea, and backache are early symptoms. The rectum can be easily and satisfactorily examined, which results in a relatively early diagnosis.

TREATMENT

Most writers have advised conservative management of these tumors.[23] Recently, however, Shepard and coworkers [12] advised a more radical treatment and gave several sound reasons for this. The experience of Stout,[9] Helwig,[23c] and Dukes [23d] would seem to obviate radical surgery if no metastasis can be found and if the local lesions are not too large to be removed easily. It is our opinion, after reviewing the literature and reviewing our case, that these tumors should be suspected by their gross appearance and should be treated conservatively if at all feasible. Ariel [24] and Klemperer [25] suggested that radiation may be effective, and Ariel [24] reported one case of carcinoid of the small bowel treated by surgical excision; however, the patient returned two months later with an abdominal mass at the operative site. This mass was irradiated; it responded well, and the patient was well two and a half years later. Ariel suggested, on the basis of this case, that carcinoids may be radiosensitive. Since some patients have lived for years with stationary metastases, it is difficult to evaluate a reaction of this type. It will be interesting, however, to follow our own case to note whether or not further metastases appear.

TABLE 2.—*Unusual Locations of Carcinoids**

Location	No. of Cases
Rectum	56
Stomach	23
Colon (exclusive of rectum)	22
Meckel's diverticulum	7
Ovarian teratoma	6
Gallbladder	3
Mesentery	2
Diverticulum (unspecified)	1

* Taken from Pautler and Scotti.[11]

SUMMARY

An unusual and uncommon case of a rectal carcinoid metastatic to the broad ligament is reported, which caused considerable speculation and concern in the identification of the first tumor nodule removed. It is our belief that this is the first reported case of malignant rectal carcinoid with known metastasis of four years' duration without spread to other organs. It is one of seven reported cases of malignant carcinoids of the rectum, and the patient in the case reported here is the youngest with proved metastasis.

It is pointed out that even the malignant carcinoids, both of the rectum and other locations, may at times have a remarkably chronic course. The frequency (64%) with which rectal carcinoids appear on the anterior wall of the rectum is mentioned. We believe, after reviewing the literature, that a rectal carcinoid should be suspected when a small tumor of the rectum is found in which the mucous membrane appears intact over the surface and that such tumors should be treated by local excision unless they are diffuse (as in Rigdon's case) or are infiltrating annular lesions (as in Pearson and Fitzgerald's case) or metastatic spread is suspected.

ADDENDUM

At the time of the last examination of this patient on May 20, 1952, 18 months after the abdominoperineal resection, she was well and apparently free of recurrent disease.

800 Medical Arts Bldg. (Dr. Epps).

22. (*a*) Horn,[8] Pearson and Fitzgerald.[10b] Stout,[9] Wilson.[13] (*b*) Ackerman, L. V.: Personal communication to the authors.

23. (*a*) Stout,[9] (*b*) Brunschwig, A.: Argentaffin Tumor (Carcinoid) of the Rectal Colon, J. A. M. A. **100**: 1171-1172 (April 15) 1933. (*c*) Helwig, E. B.: Benign Tumors of the Large Intestine—Incidence and Distribution, Surg., Gynec. & Obst. **76**: 419-426, 1943. (*d*) Dukes, C. E.: Peculiarities in the Pathology of Cancer of the Ano-Rectal Region, Proc. Roy. Soc. Med. **39**: 763-765, 1946. (*e*) Yaker, D. N.: Carcinoid of the Rectum, Clinics **3**: 1055-1058, 1944.

24. Ariel, I. M.: Argentaffin (Carcinoid) Tumors of the Small Intestine: Report of Eleven Cases and Review of the Literature, Arch. Path. **27**: 25-52 (Jan.) 1939.

25. Klemperer, P., in discussion on Goldberg, S. A.: Unusual Neoplasms of the Small Intestine, Am. J. Path. **14**: 663-664, 1938.

Yellow Fever.—Yellow fever, like typhus, is not dead in spite of all of the conquests and conquerors of this disease, nor is it likely to die out so long as the tropical and subtropical forests maintain their mammalian hosts and insect vectors. Jungle yellow fever remains as a potential source of virus for undoing the conquest of urban yellow fever, wherever Aëdes aegypti is permitted to continue, as witness the 1928-29 outbreak in Rio de Janeiro. . . . In South America, only Chile and Uruguay are free from this disease. . . . A tragic occurrence early in 1951 was an outbreak of jungle yellow fever with over 2,000 cases and several hundreds of deaths, among the newly arrived settlers in the State of Goiaz, Brazil. This area had suffered an outbreak in 1945, at which time extensive vaccination was carried out in the then relatively small population. During the past six years, however, an important agricultural development has brought in large numbers of nonimmunes from Northeast Brazil. . . . Ironically enough, these newcomers came from the previously highly endemic region of aegypti-transmitted yellow fever of Northeast Brazil, where there is no jungle yellow fever. It was here that the Rockefeller Foundation initiated its campaign in Brazil against aegypti-transmitted yellow fever in 1923, with the resultant development of this nonimmune susceptible population. . . . As the years pass and jungle yellow fever continues to be jungle yellow fever, without invasion of the cities, the potential threat seems unimportant to many who do not realize the tremendous effort which has gone, and is going, into the eradication of Aëdes aegypti in all of the towns and cities in close contact with the infected forests.—F. L. Soper, M.D., The Elephant Never Forgets, *American Journal of Tropical Medicine and Hygiene*, May, 1952.

CLINICAL NOTES

LIVER NECROSIS AND DEATH FOLLOWING HEPATIC ARTERY LIGATION

David Rosenbaum, M.D.
and
Herbert L. Egbert, M.D., Indianapolis

Recent reports, first by Rienhoff [1] and later by Berman,[2] have indicated that patients with cirrhosis complicated by esophageal varices and ascites may benefit from ligation of the hepatic artery. It has been commonly assumed previously that viability of the liver was dependent on adequate blood supply through the hepatic artery and that ligation of this vessel would result in liver necrosis and death. Markowitz, Rappaport, and Scott [3] reported that in dogs liver necrosis and death following such an operation could be avoided, in most cases, by administration of penicillin, indicating that the necrosis was probably the result of infection from the anaerobic bacteria normally present in the liver of dogs. Grindlay, Mann, and Bollman [4] recently suggested the possibility that in those animals that survived there had not been complete stoppage of the blood supply to the liver through the ligated artery or that collateral channels had been established. These recent reports of successful ligation of the hepatic artery in patients with cirrhosis suggest that in cirrhosis the blood supply to the liver has been so altered that such ligation does not result in damage to the liver and that the function of the liver may even be improved. We have recently observed a case of cirrhosis in which ligation of the hepatic artery was not tolerated and resulted in liver failure and death. This case indicates that ligation of the hepatic artery is not innocuous in all cases of cirrhosis.

REPORT OF A CASE

The patient was a white man, 40 years old, who was admitted to this hospital twice because of massive upper gastrointestinal hemorrhage. He had had an attack of jaundice at the age of 26 and a questionable attack at 34. He admitted excessive use of alcohol for several years, and for the past two or three years, he had had symptoms of indigestion, vertigo, syncope, and edema of the legs.

First Hospitalization.—The patient was first admitted to the hospital on July 12, 1950, after having passed blood in his stools and having vomited a large amount of bright red blood during the preceding four days. Physical examination revealed a soft systolic murmur heard over the entire precordium, several spider nevi over the neck and shoulders, enlargement of the liver 2 cm. below the costal margin, and a small amount of ascites. Laboratory tests made between July 12 and July 20 showed the following results: red blood cell count 2,100,000; gastric analysis showed 20 degrees of free hydrochloric acid; the blood serum contained 1.2 mg. of bilirubin, 5.7 gm. of protein, and 2.8 gm. of albumin per 100 cc.; reaction to the cephalin-cholesterol flocculation test was 2+, and to the thymol flocculation test was negative; a thymol turbidity test showed 5 units, and a zinc turbidity test, 25 units. Tests made between Aug. 20 and Aug. 30 showed the following results: the blood serum contained 0.8 mg. of bilirubin, 7.9 gm. of protein and 4.9 gm. of albumin per 100 cc.; reaction to the cephalin-cholesterol flocculation test was 3+ and to the thymol flocculation test was negative; a thymol turbidity test showed 2 units; and the sulfobromophthalein (bromosulfalein®) sodium retention in the blood was 24%. An x-ray examination revealed a large ulcer crater or pseudodiverticulum of the first portion of the duodenum. Esophagoscopic examination showed large thin-walled varices in the lower esophagus, with no evidence of recent hemorrhage.

The patient's treatment consisted of transfusions, ulcer management, and supportive therapy for cirrhosis. He had no further recurrence of bleeding and was discharged from the hospital on Sept. 5, 1950. He was seen six weeks later, at which time he complained only of mild epigastric discomfort and had had no further episodes of bleeding.

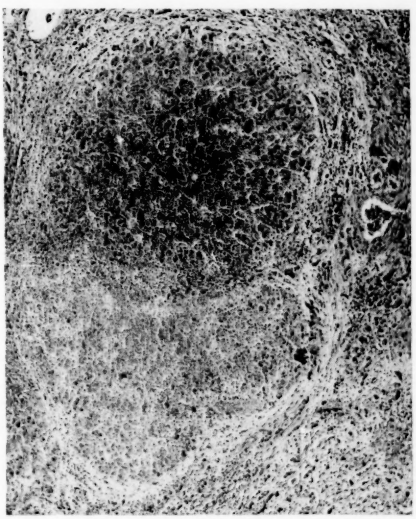

Fig. 1.—Photomicrograph of liver tissue at necropsy showing hemorrhagic infarction of cirrhotic lobule.

Second Hospitalization.—The patient was readmitted to the hospital on March 13, 1951, because of epigastric distress and hematemesis. He stated that he had had no form of treatment after his discharge from the hospital and had had frequent burning pain in the upper abdomen. He had an episode of severe bleeding in December, 1950, and again just prior to admission. Physical examination revealed spider nevi, enlargement of the liver 2 to 3 cm. below the costal margin, moderate epigastric tenderness, and gross evidence of anemia. The patient's blood pressure was 125/85 mm. Hg. An x-ray examination made several days after admission revealed a high degree of spasticity and some deformity of the duodenum. Results of laboratory tests made at this time were as follows: red blood cell count 2,200,000 to 4,000,000; total nonprotein nitrogen content of blood 54 mg. per 100 cc.; prothrombin 58 to 96% of normal; blood serum contained 1.6 mg. of bilirubin, 6.8 gm. of protein, and 3 gm. of albumin per 100 cc.; reaction to the cephalin-cholesterol flocculation test was 4+ and to the thymol flocculation test was

From the Veterans Administration Hospital, Indianapolis.

1. Reinhoff, W. F., Jr.: Ligation of the Hepatic and Splenic Arteries in the Treatment of Portal Hypertension with a Report of 6 Cases: Preliminary Report, Bull. Johns Hopkins Hosp. **88**: 368-375, 1951.

2. Berman, J. K.; Koenig, H., and Muller, L. P.: Ligation of Hepatic and Splenic Arteries in the Treatment of Portal Hypertension: Ligation in Atrophic Cirrhosis of the Liver, A. M. A. Arch. Surg. **63**: 379 (Sept.) 1951.

3. Markowitz, J.; Rappaport, A., and Scott, A. C.: The Function of the Hepatic Artery in the Dog, Am. J. Digest. Dis. **16**: 344-348, 1949.

4. Grindlay, J. H.; Mann, F. C., and Bollman, J. L.: Effect of Occlusion of the Arterial Blood Supply to the Normal Liver, A. M. A. Arch. Surg. **62**: 806-811 (June) 1951.

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negative; a zinc turbidity test showed 24 units; reaction to the colloidal red test was 4+, to the galactose tolerance test was normal, and to a serologic test for syphilis was negative. Esophagoscopic examination again revealed the presence of large, thin-walled varices in the lower esophagus, which had undergone little change since the previous examination.

Because of the recurrent hemorrhages, it was felt that the patient should have surgical treatment, although it had not been

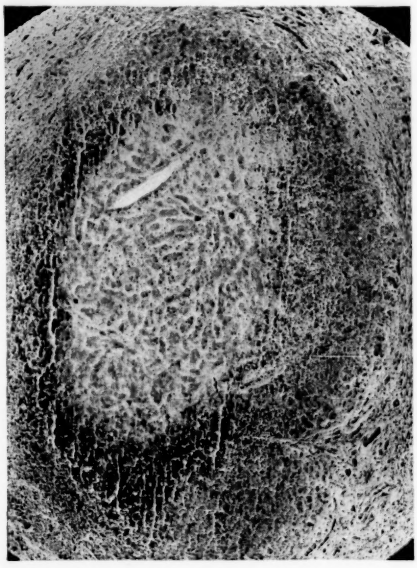

Fig. 2.—Photomicrograph of liver tissue at necropsy showing ischemic infarction of cirrhotic lobule.

determined whether the bleeding was occurring from the varices or the duodenal ulcer. The operation was done April 16, 1951, with the patient under intratracheal ether anesthesia, which lasted four hours; 2,500 cc. of blood was given during the operation. Exploration revealed considerable nodular cirrhosis and some enlargement of the liver. The spleen was about three times normal size and had no unusual adhesions to the diaphragm. There were some moderately dilated veins about the upper stomach. A great many adhesions were present about the free edge of the lesser omentum, making dissection of this area difficult and bloody. A large, posterior, penetrating duodenal ulcer, which was not actively bleeding, was present about 2 cm. from the pylorus. Measurements of portal pressure were taken in a large gastroepiploic vein, using the second lumbar vertebra as a base line; the pressure thus obtained was 430 mm. of water. Temporary occlusion of the portal vein resulted in no change in this pressure; with temporary occlusion of the hepatic artery, a fall of 10 to 20 mm. of water was observed.

It was felt that the source of the bleeding had not been determined with certainty and that prevention of further bleeding from both the duodenal ulcer and the varices should be provided. Accordingly, vagotomy and partial gastric resection were done, and, in addition, the hepatic artery was ligated just proximal to a large gastroduodenal branch. During the operation the patient's condition was fair, although his blood pressure for a long period of time was about 80/60 mm. Hg. The patient's tendency to bleed seemed to increase, and considerbale oozing was encountered, even during wound closure.

The immediate postoperative course was satisfactory. On the evening following the operation the patient's blood pressure fell, and there was considerable oozing of blood from the wound. He was given supportive treatment, with further blood transfusion, and his blood pressure rose to a normal level. On the day after the operation, he became progressively drowsier and more lethargic. In spite of administration of large amounts of vitamin K, the prothrombin level dropped to 23% of normal. The red blood cell count at this time was 4,200,000, and the serum bilirubin content was 9.2 mg. per 100 cc. The patient was treated with plasma, whole blood, vitamin K, human serum albumin, cortical extract, and cortisone, but his course was progressively downhill, with increasing jaundice and lethargy and rising temperature. He died on the second postoperative day.

Necropsy.—Necropsy was performed eight hours after death. The skin and scleras were highly jaundiced. No evidence of hemorrhage was found in the abdominal wound. There was almost 400 cc. of bloody fluid in the peritoneal cavity, and a fibrinous exudate was present over the surface of the liver and greater omentum. The lungs showed beginning bronchopneumonia and minimal edema. No definite esophageal varices could be found. The spleen was enlarged, weighing 450 gm., and appeared to be congested. The liver was enlarged, weighing 2,360 gm., and was extremely cirrhotic, with nodules of varying sizes over the surface and throughout the cut sections. Gross hemorrhage was apparent in most of these regenerated cirrhotic nodules, although occasional lobules presented a yellowish, caseous appearance, with peripheral zones of hemorrhagic discoloration. The portal vein was normal in appearance, and its lumen contained no thrombotic material. The hepatic artery was completely ligated immediately proximal to the gastroduodenal branch, and had no thrombosis, either distal to or proximal to the ligature.

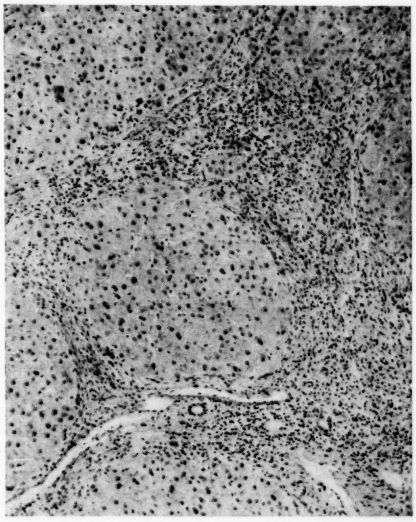

Fig. 3.—Photomicrograph of section of liver taken for biopsy during the operation for ligation of the hepatic artery showing typical portal cirrhosis with viable hepatic parenchyma.

Important microscopic changes were observed in the liver. The underlying condition was typical portal cirrhosis. The architecture was completely disrupted by broad and narrow bands of fibrous connective tissue, in which there were numerous lymphocytes and proliferated bile ducts. These interlacing bands enclosed and rather sharply demarcated lobules of regenerated hepatic parenchyma of varying sizes. In addition, recent superimposed changes of two general types were observed in the regenerated lobules. Most of the lobules were hemorrhagic, with

destruction of almost all the parenchymal cells (fig. 1). The hemorrhage tended to be more intense centrally than peripherally, and there was frequently an infiltration of polymorphonuclear leukocytes into the peripheral regions of the lobules. Within the central region, liver cords in which the nuclei had lost or partially lost their staining qualities and which were in various stages of necrosis were frequently seen. Occasional lobules showed no hemorrhage but rather extensive ischemic necrosis of the greater portion of the lobule with peripheral zones of polymorphonuclear leukocytes, which in turn were surrounded by hemorrhagic zones (fig. 2). A few of the regenerated lobules appeared to have escaped any degree of change, but even these showed marked vacuolation of the cytoplasm of the parenchymal cells. The fibrous connective tissue constituting a large portion of the liver appeared to be unaffected by recent acute change, except in one small area where a minute, irregular hemorrhage was observed. There was no evidence of necrosis or gangrene of the connective tissue itself. The regenerated bile ducts within the connective tissue septums were normal in appearance. The changes described were interpreted as hemorrhagic and ischemic infarcts due to ligation of the hepatic artery; none of these changes, except the underlying portal cirrhosis, had been observed in an adequate biopsy of the liver done at the time of the operation (fig. 3).

COMMENT

The changes observed in the liver of this patient appear to have been the direct result of interruption of the major blood supply of almost the entire liver. They were not characteristic of toxic damage to the liver following prolonged anesthesia, extensive surgery, or periods of hypotension. It seems obvious that the hepatic parenchyma was supplied with blood chiefly through the hepatic artery and that surgical ligation of this vessel resulted in widespread infarction.

In addition to the cases reported by Rienhoff and Berman, we know, personally, of a number of patients in whom ligation of the hepatic artery has been done without incident. It seems apparent that in these patients the blood supply to the liver is maintained through other pathways, including the portal vein and collateral arteries. It should be noted that in the patient described ligation was done proximal to a large gastroduodenal artery which did not serve as an adequate collateral vessel. The result of the operation in this patient indicates that circulation to cirrhotic livers must vary considerably, both from the viewpoint of the arrangement of extrahepatic arterial pathways and from the anatomical situation within the liver resulting from the more or less haphazard regeneration of liver tissue. There may even be variation in the blood supply to different parts of the same liver. We had a patient in whom ligation of the portal vein was done and whose death six days postoperatively afforded us an opportunity to examine his liver. In general, it was not affected by ligation of the portal vein, but isolated lobules scattered here and there in the liver were infarcted in exactly the same manner and with exactly the same appearance as those observed in the present patient. In this patient, it seems that the chief source of blood to the liver was the hepatic artery but that some lobules were supplied entirely or principally by the portal vein. These were the lobules that became infarcted.

It is our belief that destruction of liver cells may cause complete disorganization of normal architecture and that regeneration may be so haphazard that it is impossible to predict what will be the resultant sources of blood to the regenerated lobules. Many patients with cirrhosis may tolerate ligation of the hepatic artery very well, and yet it seems apparent that this is hazardous treatment for others. If the operation is to have widespread application, an attempt must be made to establish criteria for determining which patients may be treated in this manner without undue danger.

SUMMARY

1. A case of almost complete hepatic infarction following hepatic artery ligation in a patient with portal cirrhosis of the liver is reported.

2. It is suggested that the regenerative process in cirrhotic livers is variable and that the blood supply to the regenerated nodules is unpredictable. This hypothesis may explain the fatal consequences of hepatic artery ligation in our patient, in contrast to its apparent harmlessness in previously reported cases.

3. Development of proper criteria for selection of patients must precede the widespread use of this operation for treatment of cirrhotic patients.

1481 West 10th St. (7) (Dr. Rosenbaum).

STOMACH PAIN CAUSED BY MASKED HYDRONEPHROSIS

Ralph C. Lohrey, M.D.
George C. Poore, M.D.
and
John D. Osmond Jr., M.D., Cleveland

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"Stomach ache" in children is a complaint familiar to all physicians, but is seldom accorded the careful study that is given the same symptoms in adults. These attacks of epigastric distress occurring in childhood are usually viewed lightly and considered to be due to dietary indiscretion if no physical sign is found. The case reported here is a reminder that hydronephrosis is one cause of such abdominal pain even when no mass is palpable.

Hydronephrosis is not uncommon in childhood, but is frequently difficult to diagnose. Meredith Campbell [1] reviewed 825 cases of this disease and found that less than one-fourth of the patients had a palpable mass. Furthermore, 316 cases were discovered only at autopsy. Childhood hydronephroses usually result from anomalies of the urinary tract.[2] These include stricture, kinking of the ureter, and obstruction of the ureter by aberrant vessel, fibrous band, enlarged lymph nodes, or purulent collections. Calculi are not common. Even more rarely neuromuscular disturbances, hydrocolpos, hematocolpos, pelvic masses, and bladder diverticula are the cause of hydronephrosis.

Symptoms of hydronephrosis may be absent, but vary with the site, intensity, and duration of obstruction. In order of frequency, the signs and symptoms include pyuria, temperature elevation, pain, vomiting, frequency,

From the Departments of Pediatrics, Urology, and Radiology of The Euclid Clinic Foundation and Glenville Hospital.

1. Campbell, M. F.: Clinical Pediatric Urology, Philadelphia, W. B. Saunders Company, 1951.
2. Naegeli, F. D.: Hydronephrosis in Children, J. Lancet **71**: 182-183, 1951.

hematuria, dribbling, dysuria, enuresis, and palpable mass. Hydronephrosis is slightly more frequent in females and on the left side.

REPORT OF A CASE

K. G., a 7-year-old girl, was first seen for the present illness on June 4, 1951. The chief complaint was "stomach ache," which had first been noted two years before. During the interim the patient had six distinct episodes of pain that lasted about one-half hour. They occurred at various times of the day and night, and each was finally relieved by vomiting. The most recent attack had been on May 21, 1951. There was no associated disturbance of the urinary or sleep pattern. The patient's appetite was fair, and growth had been normal. The past and family histories were noncontributory.

Physical examination showed a slender, alert, pale girl who did not appear malnourished, chronically ill, or underdeveloped. Slight silver wire changes were seen in the ocular fundi. No abnormality was found in the heart. The blood pressure was 118/74 mm. Hg. The abdomen was soft, and no mass was palpable. Slight tenderness was suggested in the upper left quadrant.

Before the diagnostic study could be completed the patient had another similar attack during the night of June 7, 1951. The episode ended with four emeses. Following this there was no distress or temperature elevation. During the examination performed the next morning the lower pole of the left kidney and tip of the spleen were palpable. The only tender area noted was in the region of a mass medial to the left kidney.

Results of urinalysis were negative except for a rare leukocyte seen in the centrifuged sediment. The red blood count was 3,930,000 and the white count 12,600. The hemoglobin level was 68% of normal (Sahli). No abnormal change was present in the electrocardiogram.

Radiographic study of the chest and abdomen did not show any pathological change. The barium study of the upper gastrointestinal tract showed the stomach to be larger than average and to contain a small residue of gastric secretion. A moderate-sized extrinsic pressure defect was noted posterior to the midportion of the stomach. This mass was thought to be in the kidney or pancreas (figure, *A*). The excretory urogram (figure, *B*) revealed a moderate left hydronephrosis. The obstruction was at the ureteropelvic junction and was considered to be due to an aberrant vessel or a fibrous band. The right kidney, ureter and bladder were normal.

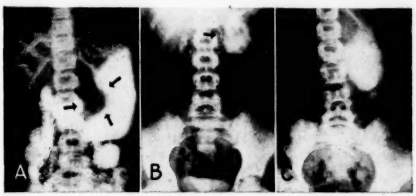
With the patient under thiopental (pentothal®) anesthesia, retrograde urography was performed using the no. 16 French Brown Buerger cystoscope. The urethra and bladder were normal. The left ureter was readily catheterized for 15 cm., at which point a hydronephrotic drip of clear, pale, yellow urine came through the no. 5 French ureteral catheter. The capacity of the pelvis was estimated at over 100 cc., so this was replaced with a similar amount of iodopyracet (diodrast®) compound solution and pyelograms were obtained with the patient supine and erect (figure). These confirmed our previous impression of a fixed ureteropelvic obstruction, with a resultant hydronephrosis made more severe by the angulation produced in the erect position.

On July 27, 1951, with the patient under gas, oxygen, and ether anesthesia, the left kidney was exposed via a left lumbar incision of the Israel type. The kidney was found to have a short pedicle with a large accessory vein to the lower pole. Although otherwise freely movable, the kidney was anchored in position by this lower pedicle. In the recumbent position the abnormal vessel compressed the uretropelvic junction moderately. This intermittent obstruction had produced the severe distention of the renal pelvis that caused the deformity of the stomach. The hydronephrosis was so extensive that it was felt no plastic operation was justified. Since there was a normal system on the right, nephrectomy and partial ureterectomy were performed. The wound was closed without drainage. Chromic gut was used for the muscles and silk for the skin.

The surgical specimen was examined by Dr. Lester Adelson, who reported that the specimen was a kidney with 3 cm. of ureter attached, measuring 10 by 4 cm. and weighing 80 gm. The capsule stripped readily, leaving a smooth, shiny, pale, light brown surface. The cross section revealed a clear corticomedullary demarcation. The cortex measured 5 mm. in average width. The renal pelvis and the calices were markedly dilated. The mucous membrane of the pelvis was intact and somewhat thickened. There was no evidence of obstructive process in any part of the ureter. The microscopic section revealed good preservation of the renal parenchyma, with glomerular and tubular structures showing no abnormality in structure. The renal pelvis was lined by orderly transitional epithelium. There was some round cell infiltration of the ureteral stroma. The diagnosis was left-sided hydronephrosis.

The postoperative course was uneventful. The diet was promptly advanced from fluids to regular type. The patient was out of bed on the second postoperative day, and thereafter needed only mild sedation for discomfort. Prophylactic intramuscular penicillin therapy was continued for six days following the operation. The patient was discharged on Aug. 8, 1951.

A recheck barium study of the upper gastrointestinal tract showed no evidence of the extrinsic pressure mass that had been caused by the hydronephrotic left kidney. Three months after the operation the patient was reexamined. There had been no recurrence of the epigastric pain or emesis since removal of the left kidney. The urinalysis and blood urea nitrogen were normal. The patient's appetite had improved, and she had a much happier attitude.



A, anteroposterior radiograph of the barium-filled stomach showing the defect of the lesser curvature aspect of the midportion, due to the hydronephrotic left kidney. *B*, excretory urogram showing the moderate left hydronephrosis. *C*, radiograph of the hydronephrotic left kidney made following retrograde injection of over 100 cc. of iodopyracet (diodrast®) compound solution. The obstruction at the ureteropelvic junction was due to an aberrant vessel.

SUMMARY

A case of "stomach ache" in a 7-year-old girl caused by left-sided hydronephrosis has been reported. Hydronephrosis had not been suspected as the cause, but was suggested by the presence of an extrinsic pressure defect discovered during barium study of the upper gastrointestinal tract. Excretory and retrograde urographic studies confirmed the diagnosis, and suggested an aberrant vessel as the cause of the obstruction. Nephrectomy was necessary because of the renal damage produced by the chronicity of the lesion.

18599 Lake Shore Blvd. (19) (Dr. Osmond).

The First Part of the Duodenum.—The first duodenal segment varies greatly in its site, shape, length, diameter, and relations. It is thick-walled yet friable. It has a profuse blood-supply, and is often supplied by extra vessels from unusual sources in addition to those embryologically expected and anatomically described. It receives the most powerful and potentially destructive ferments in the body. It is deeply placed and when diseased may present a guileless appearance that lures the surgeon on to a point from which neither advance nor retreat is possible. It is a hateful little tube but one that we must constantly attack and therefore should study as carefully as a wise general studies his enemies before battle.—Sir Heneage Ogilvie, The First Part of the Duodenum, *Lancet*, May 31, 1952.

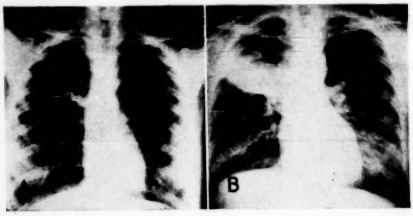
EXACERBATION OF TUBERCULOSIS DURING TREATMENT WITH CORTISONE

Eugene F. Traut, M.D., Oak Park, Ill.
and
Jerome Ellman, M.D., Chicago

Observations of the unfavorable effects of corticotropin (ACTH) and cortisone on tuberculosis are multiplying. Guinea pigs and rats taking these drugs have succumbed to doses of tubercle bacilli found nonlethal in controls.[1] Pulmonary tuberculosis in humans has also disseminated during steroid administration.[2]

REPORT OF A CASE

S. M., a 37-year-old Negro woman, was seen in the arthritis clinic of Cook County Hospital in July, 1950, because of rheumatoid arthritis of five years' duration. The arthritis, involving all four extremities, was so severe that she was barely able to walk with help. The laboratory tests revealed the presence of hypochromic anemia and an accelerated erythrocyte sedimentation rate, findings commonly encountered in severe rheumatoid arthritis. She had no symptoms referable to the respiratory tract nor abnormal physical findings in the lungs. During case-finding studies she had previously had x-ray studies of her lungs. During two admissions to another hospital for treatment of the arthritis,



A, roentgenogram of the chest showing infiltration in the upper lobe of the right lung before cortisone therapy in May, 1950. *B*, roentgenogram showing marked spread of the lesion during cortisone therapy in January, 1951.

routine roentgenograms had been made. She had never been told that these indicated pulmonary disease. She had never suspected any lung abnormality until, following discharge from Cook County Hospital in June, 1950, a visiting nurse had advised her to have x-ray studies of her lungs each six months. No reason for this advice was advanced.

On admission to Cook County Hospital in September, 1950, she was give cortisone (cortone® [Merck]) orally in doses of 300 mg. the first day, 200 mg. the second day, and 100 mg. daily thereafter. Within 24 hours there was a marked decrease in all the symptoms and signs of arthritis. Her appetite, strength and spirits rose correspondingly. Her weight increased 2 lb. (0.9 kg.) within four weeks. There was no demonstrable edema.

Symptoms of a "cold" developed in the 12th week of cortisone therapy. Cough, fever, and expectoration persisted. The patient complained of night sweats. Tubercle bacilli were found in the sputum, and marked extension of the tuberculosis was demonstrated roentgenologically (figure).

Administration of cortisone was discontinued, and the arthritis was temporarily much worse. Subsequently and concurrently with the bed rest enforced because of the tuberculosis, remission of the arthritis has occurred. The roentgenologic evidences of tuberculosis remain the same. The temperature is normal, and there is no cough nor production of sputum.

I have other patients with arrested pulmonary tuberculosis who are receiving cortisone for crippling rheumatoid arthritis without any apparent increase in their pulmonary infection.

CONCLUSION

Patients who are to receive corticotropin (ACTH) or cortisone should be examined for tuberculosis, including by roentgenologic studies. Any findings that suggest the presence of tuberculosis should be carefully and frequently reviewed for possible activation during treatment with corticotropin or cortisone. The presence of pulmonary tuberculosis may contraindicate the use of corticotropin or cortisone.

715 Lake St. (Dr. Traut).

1. (*a*) Michael, M., Jr.; Cummings, M. M., and Bloom, W. L.: Course of Experimental Tuberculosis in the Albino Rat as Influenced by Cortisone, Proc. Soc. Exper. Biol. & Med. **75**: 613 (Nov.) 1950. (*b*) Freeman, S.; Fershing, J.; Wang, C. C., and Smith, L. C.: Effect of ACTH on Patients with Pulmonary Tuberculosis in Clinical ACTH Conference, Proceedings of the First Meeting, edited by J. R. Mote, Philadelphia, The Blakiston Company, 1950, p. 509.

2. King, E. Q.; Johnson, J. B.; Batten, G. S., and Henry, W. L.: Clinical Notes: Tuberculosis Following Cortisone Therapy: Report of a Case of Rapidly Progressive Pulmonary Tuberculosis Following Cortisone Therapy for Rheumatoid Arthritis, J. A. M. A. **147**: 238 (Sept. 15) 1951. Popp, C. G.; Ottosen, P., and Brasher, C. A.: Cortisone and Pulmonary Tuberculosis, ibid. **147**: 241 (Sept. 15) 1951. Fred, L.; Levin, M. H.; Rivo, J. B., and Barrett, T. F.: Development of Active Pulmonary Tuberculosis During ACTH and Cortisone Therapy, ibid. **147**: 242 (Sept. 15) 1951. Freeman and others.[1b]

TESTICULAR ANDROGEN DEFICIENCY AND SEMEN VOLUME

E. Perry McCullagh, M.D.
and
C. A. Schaffenburg, M.D., Cleveland

The assessment of androgenic activity in male subjects by simple and easily accessible methods is highly desirable. Tests such as the determination of 17-ketosteroids and urinary gonadotropins are not readily available to the general practitioner. Also, the proper clinical evaluation of the secondary sex characteristics (e. g., frontotemporal recession of the hairline, the beard, and pubic and axillary hair) requires familiarity with these signs, and they have the disadvantage of not relating directly to the levels of androgens circulating at the time of examination. We wish, therefore, to call attention to the use of semen volume measurements as an index of androgenic function.

There are, as Huggins [1] pointed out, two different types of male secondary sex characteristics: the self-maintaining (such as beard and voice pitch), which once developed will not atrophy in the absence of androgen, and those depending strictly on a constant presence of this hormone for the maintenance of their anatomic and functional integrity. In the latter category are the sex accessories, such as prostate and seminal vesicles. From this it follows that any serious decrease in the amount of circulating androgen will be reflected in the sex accessories and, therefore, in semen.

Semen is composed of two parts: (1) the spermatozoa, produced by the seminiferous tubules, and (2) the plasma, produced by the sex accessories where prostate and seminal vesicles contribute the largest portion. When there is failure of the seminiferous tubules (or

From the Cleveland Clinic and the Frank E. Bunts Educational Institute.

1. Huggins, C.: Prostatic Secretion, Harvey Lect. (1946-1947) **42**: 148, 1947.

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mechanical obstruction distad to them) there may be oligospermia or even azoospermia. However, if Leydig cell function is preserved, as is often the case, semen volume is normal, since the sex accessories are receiving an adequate androgen supply.

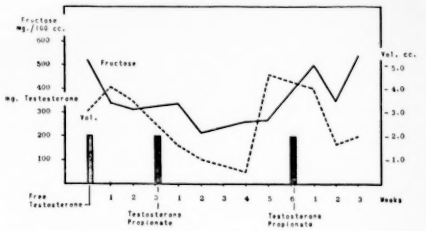
There are in plasma a number of chemical substances, characteristic of different portions of the sex accessories, the concentration of which depends on the amount of circulating androgen. In man, the enzyme "acid" phosphatase is elaborated in the prostate [2] and a sugar, fructose, in the seminal vesicles. Both of these substances have been variously utilized as an index of androgenic function.[3] Fructose concentration parallels semen volume up to amounts of 4 to 5 cc. Above this its concentration decreases.[3e] In the accompanying table we have plotted the average fructose concentration in milligrams per 100 cc. of semen as related to the volume of several specimens obtained from patients with hypogonadism treated with testosterone preparations. It will be noted that fructose concentrations increase proportionately with semen volume although the range of variation is great. In some men fructose concentration shows an inverse relationship to semen volume. This is exemplified in the accompanying figure.

Recently Landau and Loughead [4] utilized fructose measurements as an index of androgen activity in eunuchoid or normal persons. In our hands fructose determinations have proved to be no more valid indexes of androgenicity than the semen volume alone. The reasons for this are that the normal individual variations are large (from about 200 mg. per 100 cc. to 800 mg. per 100 cc.) and that there are no significant changes in fructose concentration in the absence of changes in semen volume. In severe, untreated eunuchoidism, the subject is incapable of erection or ejaculation or the semen volume is extremely low (0.1 cc. or less). When androgen is administered the volume gradually increases until it reaches a normal level. Semen specimens should be obtained after four days of continence; in these conditions normal

Relationship of Fructose Concentration to Semen Volume in Azoospermic, Eunuchoid Patients Treated with Testosterone

No. of Patients	No. of Specimens	Vol. (Cc.)	Fructose Concentration, Mg. per 100 Cc.	Range
6.....	23	1.0 or less	192	45-560
5.....	31	1.1-2.0	331.8	170-585
7.....	21	2.1-3.0	427.1	155-615
5.....	27	3.1-4.0	434.2	215-655
4.....	13	4.1-5.0	529.2	270-740

semen volumes vary from 2 to 7 cc. Volumes of more than 3 cc. on repeated examinations and especially volumes over 5 cc. can be considered good evidence that there is no deficiency of circulating androgen. Amounts of less than 2 cc. on repeated occasions raise the suspicion of androgen deficiency. If this has developed in a fully matured person, other signs may not be evident. A more thorough endocrine investigation is then warranted.



Cryptorchism with eunuchoidism: effect of testosterone propionate therapy on semen volume and semen fructose concentration.

SUMMARY

Attention is called to the fact that in clinical practice the simple procedure of measurement of semen volume may be used to advantage as a screening test for hypogonadism insofar as it relates to testicular androgen production.

2020 E. 93d St.

RECURRENT NATURE OF ACUTE BENIGN PERICARDITIS

Clyde E. Tomlin, M.D.
R. Bruce Logue, M.D.
and
J. Willis Hurst, M.D., Emory University, Ga.

Despite the extensive literature relating to acute benign pericarditis and the observation of recurrent attacks by various writers,[1] the high incidence and the frequency of recurrences in this illness have not been stressed. It is the purpose of this paper to emphasize this point by presenting a detailed report of one patient and summarized data for eight patients, in whom such episodes of acute benign pericarditis occurred (see the accompanying table). The following case, in which the largest number of recurrences was observed, is presented as an example of this group.

From the Department of Cardiology, Emory University School of Medicine.

2. Huggins,[a] Mann, T., and Lutwak-Mann, C.: Secretory Function of Male Accessory Organs of Reproduction in Mammals, Physiol. Rev. **31**: 27 (Jan.) 1951.

3. (*a*) Clark, L. C., Jr.; Beck, E. I., and Thompson, H.: Excretion of Acid Phosphatase as Measure of Prostatic Development During Pubescence, J. Clin. Endocrinol. **11**: 84 (Jan.) 1951. (*b*) Engberg, H.; Andersson, E.; Sury, B., and Raft, J.: Possibility of Determining Androgen Production by Measuring Acid Phosphatase in Semen: Investigations in Cryptorchid Patients, ibid. **5**: 42 (Feb.) 1947. (*c*) Harvey, C.: Relation Between Volume and Fructose Content of Human Semen, Nature **162**: 812 (Nov. 20) 1948. (*d*) Lundquist, F.: Aspects of Biochemistry of Human Semen, Acta physiol. scandinav. (supp. 66) **19**: 7, 1949.

4. Landau, R. L., and Loughead, R.: Seminal Activity in Man, J. Clin. Endocrinol. **11**: 1411 (Dec.) 1951.

1. (*a*) Burchell, H. B.: Acute Nonspecific Pericarditis, Mod. Concepts Cardiovas. Dis. **16**: [n.p.] (March) 1947. (*b*) Logue, R. B., and Wendkos, M. H. Acute Pericarditis of Benign Type, Am. Heart J. **36**: 587-599 (Oct.) 1948. (*c*) Barnes, A. R., and Burchell, H. B.: Acute Pericarditis Simulating Acute Coronary Occlusion, ibid. **23**: 247-268 (Feb.) 1942. (*d*) Wolff, L.: Acute Pericarditis Simulating Myocardial Infarction, New England J. Med. **230**: 422-425 (April 6) 1944. (*e*) Massey, F. C.: Acute Pericarditis Simulating Myocardial Infarction, Northwest Med. **46**: 455-459 (June) 1947. (*f*) Feder, I. A.; Hoffman, J., and Sugar, H.: Acute Primary Pericarditis, Am. J. M. Sc. **220**: 144-155 (Aug.) 1950. (*g*) Evans, E.: Acute Nonspecific Benign Pericarditis, J. A. M. A. **143**: 954-957 (July 15) 1950. (*h*) Carmichael, D. B.; Sprague, H. B.; Wyman, S. M., and Bland, E. F.: Acute Nonspecific Pericarditis: Clinical, Laboratory, and Follow-up Consideration, Circulation **3**: 31-331 (March) 1951. (*i*) Levy, R. L., and Patterson, M. C.: Acute Serofibrinous Pericarditis of Undetermined Cause: Study of 27 Cases, Am. J. Med. **8**: 34-45 (Jan.) 1950.

REPORT OF A CASE

F. J. G., a 27-year-old white woman, a registered nurse, was admitted to the hospital on July 21, 1950, with the chief complaint of sudden onset of severe substernal and precordial pain, accentuated by inspiration and by lying in the supine position but not increased by swallowing. She had her first attack of such pain at the age of 6 years; 19 subsequent attacks occurred. The longest interval between recurrences was four years. Occasionally respiratory infection preceded an attack. Results of physical examination were normal except for temperature of 100.4 F. The cardiac rhythm was regular. There was no murmur, rub, or gallop rhythm. Examination of the lungs revealed no abnormality. There was no mediastinal crepitation.

The sedimentation rate was 24 mm. per hour (Westergren). The white blood cell count was 10,650 per cubic millimeter, with a normal differential count. Roentgenograms of the gallbladder, gastrointestinal tract, cervical and thoracic spine, and chest were normal. Results of fluoroscopic examination of the chest were normal. The electrocardiogram revealed shortening of the T vector in the frontal plane with isoelectric T waves in V_5 and V_6. The patient had low-grade fever for two days. The pain gradually disappeared, and she was asymptomatic when she was discharged, on the fourth hospital day.

One month later the same symptoms reappeared. Physical examination revealed a faint pericardial friction rub in the fourth anterior intercostal space in the midclavicular line. Her temperature was 99.2 F. An electrocardiogram taken five hours after the onset of the pain revealed marked lowering of the T waves in all leads. The use of narcotics was necessary for the relief of the pain, and she was asymptomatic in six days. The patient was subsequently hospitalized elsewhere on two occasions because of recurrence of the same symptoms.

COMMENT

The symptoms, physical findings, laboratory data, and the electrocardiographic changes have been discussed elsewhere.[2] The pain is usually substernal or precordial, and from the onset the striking characteristic of the pain is its close relationship to inspiration, bodily movements, cough, and sometimes swallowing. Occasionally the patient may be acutely ill and may present the picture of peripheral collapse. Frequent examinations may be necessary for the detection of the pericardial friction rub. Cardiac dilatation is believed by some to occur,[3] but the increase in the cardiac silhouette is more likely due to pericardial effusion, which is probably present in small amounts in most cases.[4] Pleural effusion may at times be noted.

In acute benign pericarditis an injury current due to diffuse subepicardial myocarditis is reflected on the electrocardiogram as concave S-T segment elevation in one or more leads.[1b] It is important to differentiate these changes from the persistent S-T elevation seen occasionally in normal subjects having T vectors of large magnitude, with early forces of repolarization giving rise to S-T elevation. The T waves may be tall and peaked at the onset, but after a short time they are flattened and later may become inverted. The T-wave changes may be

Summary of Data

Patient	Age, Yr.	Sex	Antecedent Infection	No. of Recurrences	Chill	Character of Pain
J. H.	34	M	Measles 3 weeks prior to first attack	3 (1) 1942 (2) 1948 (3) 1949	....	Severe substernal, radiating to shoulder, lasting 10 days, not relieved by glyceryl trinitrate therapy, aggravated by deep breathing, movement, and walking
H. W.	33	M	Acute sinusitis 10 days prior to first attack	4 (1) 1948 (2) 1948 (3) 1949 (4) 1950	Yes	Epigastric and substernal, stabbing, radiating to neck, arms, fingers, aggravated by movement, swallowing, breathing; patient acutely ill
R. I.	25	M	None	9 between Nov., 1950, and May, 1951	No	Dysphagia, pain radiating from pharynx to left shoulder
F. J. G.	27	F	Occasional infection	19 since age of 6 yr.	No	Sharp, substernal and precordial pain, aggravated by cough, movement, and respiration
M. M. B.	45	F	None	8 between 1945 and 1949	Yes	Intermittent sharp, midsternal pain, radiating to arms; constant dull ache; patient acutely ill; sat upright
W. F. G.	50	M	None	2	Yes	Sudden, severe substernal, nonradiating pain aggravated by respiration, movement, and swallowing; acutely ill; intravenous use of morphine required
Case No. 14 [1b]	25	M	None	History of attack 1 yr. previously	....	Sharp precordial pain, aggravated by inspiration, coughing, and turning
Case No. 15 [1b]	46	M	Upper respiratory infection for 1 mo.	4	No	Pain in left shoulder, anterior chest, neck, increased by movement, cough, and sneezing

* Rourke-Ernstene method.

2. (*a*) Burchell.[1a] Wolff.[1d] Carmichael and others.[1b] (*b*) Nay, R. M., and Boyer, N. H.: Acute Pericarditis in Young Adults, Am. Heart J. **32**: 222-233 (Aug.) 1946.

3. (*a*) Barnes and Burchell.[1c] Levy and Patterson.[1i] (*b*) Wolff, L.: Acute Pericarditis with Special Reference to Changes in Heart Size, New England J. Med. **229**: 423-431 (Sept. 9) 1943.

4. (*a*) Porter, W. B.; Clark, O., and Porter, R. R.: Nonspecific Benign Pericarditis, J. A. M. A. **144**: 749-753 (Oct. 28) 1950. (*b*) Nathan, D. A., and Dathe, R. A.: Pericarditis with Effusion Following Infections of the Upper Respiratory Tract, Am. Heart J. **31**: 115-130 (Feb.) 1946.

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the only electrocardiographic abnormality present. QRS abnormalities do not occur.

Of most importance in the differential diagnosis is myocardial infarction. The early appearance of the pain of pericarditis and the fever and pericardial friction rub without electrocardiographic changes of myocardial infarction help establish the diagnosis of acute benign pericarditis. Tuberculous pericarditis is more often painless, and the onset is usually gradual, associated with antecedent weakness, night sweats, fever, and weight loss. The pericarditis of rheumatic fever is almost always associated with signs of myocardiitis, which are not seen in patients with acute benign pericarditis. Nay and Boyer have stressed the importance of coincident joint manifestations and leukocytosis in acute pericarditis due to rheumatic fever.[2b]

The cause of acute benign pericarditis remains obscure. In some cases it is possible to elicit a history of preceding infection, usually in the upper respiratory tract.[5] Acute benign pericarditis is sometimes seen in association with atypical pneumonia.[6] Barnes and Burchell stated the belief that occasionally a young adult may have a benign, apparently self-limited form of pericarditis, which may possibly have been due to tuberculosis.[1c] Nathan and Dathe suggested a hypersensitive response to an offending organism as a possible causative factor.[4b] It would seem more likely that the disease is due to a virus infection. If there is an immunologic response on the part of the host, it would appear to be a transitory one, in view of the repeated attacks in some patients.

The present treatment is symptomatic. Bed rest is recommended for one week, with gradual increase in activity over a period of two to three weeks. Various antibiotics,[7] chemotherapeutic agents,[6b] and antihistaminic drugs [8] have been used in the treatment of the disease, but their evaluation is difficult because the natural course of the illness is toward recovery. Taubenhaus and Brams expressed the opinion that the improvement noted in their three patients treated with aureomycin was prompt and impressive enough to warrant its further use.[9] One of our patients received aureomycin for five days during a recurrence, and another received terramycin for seven days. The pain subsided coincidentally with the administration of these antibiotics, but we do not believe that it is possible to attach any significance to this. During one acute attack the patient described above received 50 mg. of corticotropin (ACTH) without any relief of the pain.

Although further study and observation of cases will be needed before definite conclusions can be drawn, it is

in Eight Cases

Friction Rub	Pulse Rate	Maximum Temperature (F)	Maximum White Blood Cell Count	Maximum Sedimentation Rate	Chest Roentgenographic Observations	Electrocardiographic Changes: S-T Segment	Electrocardiographic Changes: T Wave
History of rub with 1st attack	70	Low-grade fever for 2 days	.....	..	.....	Elevated in all leads	Inverted in leads 1, V_5, and V_6
With first attack only	70-100	100.8	11,800	52	Small amount of fluid in costophrenic angles; cardiac silhouette normal	Elevated in leads 1 and 2, depressed in 3	.....
Present	100	.....	8,000	15	Cardiac enlargement; infiltration in left base, with fluid	.....	.....
Faint during one attack	100	100.4	10,650	24	Normal	.....	Very low in all leads
.....	100	103	12,900	4	Small amount of fluid in left costophrenic angle	Slightly elevated in leads 2 and 3	Inverted in lead 1; isoelectric in 2 and 3
Yes	84	102.2	19,100	28	Normal except for slight cardiac enlargement	Elevated in leads 1, 2, 3, and V_4-V_6	Flattened in lead 1 and in left precordial leads
Yes	...	100.2	.....	0.8*	.....	Elevated in leads 1, 2, and 3	Inverted in leads 1, 2, 3, and CF_4
Yes	108	.....	10,450	1.2*	Obliteration of left costophrenic angle; apical pleural thickening	Elevated in leads 2, 3, and CF_4	Flattened in leads 1, 2, and 3; later inverted in 1, 2, and CF_4

5. Barnes and Burchell.[1c] Evans.[1c] Levy and Patterson.[1i] Porter, Clark, and Porter.[4a] Nathan and Dathe.[4b] Willius, F. A.: Cardiac Clinics: Clinic on Acute Serofibrinous Pericarditis Secondary to Acute Pharyngitis: Comment, Treatment, Course, Proc. Staff Meet., Mayo Clin. **9**: 637-640 (Oct. 17) 1934.

6. (*a*) Wolff.[3d] Wolff.[3b] (*b*) Finkelstein, D., and Klainer, M. J.: Pericarditis Associated with Primary Atypical Pneumonia, Am. Heart J. **28**: 385-394 (Sept.) 1944.

7. Evans.[1c] Porter, Clark, and Porter.[4a]

8. Zivitz, N., and Oshlag, J. A.: Eosinophilic Pleural Effusion and Pericarditis with Effusion in Allergic Subject, J. Allergy **20**: 136-143 (March) 1949.

9. Taubenhaus, M., and Brams, W. A.: Treatment of Acute Nonspecific Pericarditis with Aureomycin, J. A. M. A. **142**: 973-975 (April 1) 1950.

generally believed that the prognosis for patients with acute benign pericarditis is good and that constrictive pericarditis does not occur. Of a series of 27 patients with acute benign pericarditis described by Levy and Patterson, 23 were reexamined at intervals of 6 months to 16 years following the acute illness.[11] All showed complete recovery without sequelae. Barnes and Burchell followed 14 patients, none of whom has shown residual damage from previous pericarditis.[10] The patient described above, after having experienced 19 attacks of acute benign pericarditis over a period of 19 years, showed no evidence of residual damage at the time of last examination.

SUMMARY

The recurrent nature of acute benign pericarditis is emphasized. A report of a case and summarized data in a series of eight cases of the disease, in which the number of recurrences ranged from 2 to 19, are presented. The clinical aspects of the disease are briefly reviewed.

10. Footnote 1 *a* and *c*.

SEGMENTAL FORCEPS

Richard H. Overholt, M.D., Boston

A special forceps has been designed for use on the uncovered surface and edge of pulmonary segments. The new segmental forceps has a narrow bite with fine-tooth edges. The shafts are flared above the tip, which automatically throws the loop of thread down over its end and into lung tissue as the knot is tightened. The possibility of including the tip of the instrument in the ligature is eliminated (fig. 1).

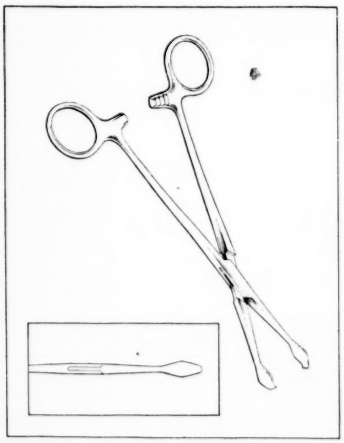

Fig. 1.—Segmental forceps, showing the shafts flared above the tips.

In sealing air leaks on segmental surfaces devoid of pleura, there is a need to grasp small amounts of tissue about the point of escape of air and to set a circumferential ligature beyond the point of the instrument (fig. 2*B*). The lung must be expanded to prove air tightness, and leaks should be sealed with segments in their normal state of inflation. If a leak is present, needle suturing produces more leaks. Ordinary hemostats, either straight or curved, gather up too much tissue, thus tending to reduce the volume of the segment and deform its surface.

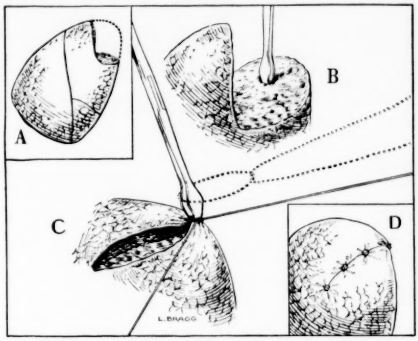

Fig. 2.—Uses of segmental forceps. *A*, apical segments after enucleation. *B*, forceps grasping small amounts of tissue to seal air leaks. *C*, segments grasped by forceps, showing ligature in position. *D*, segments anchored with ligatures.

The segmental forceps has a second use; namely, the approximation of the edges of segments or lobes. Whenever possible, it is desirable to bring two denuded segmental surfaces together; for example, after enucleation of an apical segment (fig. 2*A*), the surfaces of the anterior and posterior segments can be brought together by fastening edges at three or four points. This should be done with the segments fully inflated (fig. 2*C* and *D*).

It is also desirable to anchor a single remaining segment of one lobe to the adjacent intact lobe. This can be done by a slight shift in its position with abutment of the denuded surface of the segment against the interlobar surface of the intact lobe. This prevents rotation of the single segment, aids in sealing small air leaks, and minimizes the formation of adhesions between lung and chest wall. The fastening of segment to lobe must be done when they are inflated. The segmental forceps grasps the edge of each at three or four sites, and the tissue included in each bite is anchored with a ligature, which slips over the end of the instrument.

1101 Beacon St. (Brookline, Mass.).

The forceps was manufactured by Codman & Shurtleff, Inc., 104 Brookline Ave., Boston.

From the Department of Surgery, Tufts College Medical School, Boston. Member of the staff of New England Deaconess Hospital and New England Center Hospital, Boston.

Brain Growth.—The human skull yields to the normal outward push of the growing brain during infancy and earliest childhood. At this period, therefore, brain injury or brain destruction results in overlying cranial smallness. The rate of growth is astonishingly rapid at first for the brain increases from an average weight of 300 gm. at birth to 500 gm. at six months. At two years the weight may normally reach 900 gm., and at puberty 1,200 gm., after which there is ordinarily an increase of no more than 100 gm.—Wilder Penfield, M.D., Cranial Clues to Intracranial Abnormality, *The American Journal of Roentgenology*, April, 1952.

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THROMBOCYTOPENIC PURPURA INDUCED BY SULFISOXAZOLE (GANTRISIN®) THERAPY

REPORT OF A CASE CONTROLLED BY PLATELET TRANSFUSION

Jacob Geiger, M.D., New York

Sulfisoxazole (gantrisin®), 3,4-dimethyl-5-sulfanilamido-isoxazole, introduced in 1946, is widely used in treatment of bacterial infections, especially those of the urinary tract. The drug is said to be one of the safest of the sulfonamides. It is described by the manufacturer as a "single drug—not a mixture of several sulfonamides—so that there is less likelihood of sensitization" and as "having greater solubility and higher blood-levels." As is the case with other members of the sulfonamide group, however, reports of toxic reactions have appeared in the literature. Aside from reports of nausea, vomiting, headache, fever, and dermatitis, a number of instances of toxic effects on the bone marrow have been reported. Haunz, Cardy, and Graham [1] collected eight cases of leukopenia following the use of gantrisin,* and recently Hagerman and Franzblau [2] added another. A careful search of the literature for cases of hemorrhagic manifestations of toxicity has yielded one report [3]—that of a case of petechial hemorrhages following the administration of gantrisin,* 75.5 gm. given over a period of 12 days. In this instance there was moderate leukopenia but no thrombocytopenia. The present case is of interest because of the occurrence of toxic thrombocytopenia with its sequelae and the dramatic response following cessation of treatment with the drug and one transfusion of blood platelets.

REPORT OF A CASE

P. C., a 69-year-old man, was admitted to the hospital on Nov. 25, 1951, with a history of difficulty in voiding for the past two years. During this period he had received hormone injections. The past history revealed an episode of precordial pain with syncope about 10 years previously but was otherwise irrelevant. Results of the physical examination were normal, except with respect to the prostate, which was firm, irregular and diffusely enlarged. X-ray examination of the lumbar portion of the spine and the pelvis showed no evidence of neoplastic metastasis. The preoperative diagnosis was prostatic obstruction possibly due to carcinoma. On Dec. 3, a bilateral vasectomy and transurethral prostatectomy were performed with the patient under general anesthesia. Histological examination showed a carcinoma of the prostate. The patient reacted well. Medication consisted of the administration of sedatives, when indicated, and gantrisin,* 1 gm. three times daily, given from Nov. 25 to Dec. 4 (a total of 21 gm.). Penicillin had been ordered but was not given because the patient stated he was allergic to it. On the morning of Dec. 4, the first postoperative day, edema and what appeared to be purpuric spots on both ankles and hematuria were noted. Within a few hours, when I saw the patient, the rash had become distinctly purpuric, extending over the lower and upper extremities. There was bleeding from both nostrils and the mouth, with severe hematuria and bloody stools. The diagnosis of toxic thrombocytopenia induced by the use of gantrisin* seemed justifiable, and treatment with the drug was discontinued. Hematological examinations and a sternal bone marrow biopsy were made while the patient was being prepared for transfusion. Five hundred cubic centimeters of whole blood (18 hours old) was administered an hour later. The condition remained unchanged for the next 24 hours. Bladder irrigation yielded large blood clots; bleeding from two areas on the inside of the cheeks and from the nose continued. In the meantime a platelet concentrate was prepared from 5 units of fresh blood.[4] At 5 p. m. on Dec. 5 the patient received a transfusion consisting of approximately 450 billion blood platelets suspended in 3000 cc. of isotonic sodium chloride solution. Three hours later the bladder washings were considerably less bloody, yielding only a few small clots. Hematological findings indicated pronounced improvement, and it was the general feeling, both from a clinical and laboratory standpoint, that effective hemostasis had been established and that further hemotherapy was not indicated. On Dec. 7, the urine was grossly clear, the mouth lesions had not bled for two days, and there was gradual fading of the purpuric rash. On Dec. 10 the patient was out of bed. He was discharged on Dec. 12 in good condition.

Results of Blood Studies from Onset of Thrombocytopenic Purpura *

		Dec. 4		Dec. 5†		Dec. 6	Dec. 7	Dec. 10	Dec. 11
Date	Nov. 23	3 P.M.	4 P.M.	10 A.M.	7:30 P.M.	10 A.M.	10 A.M.	10 A.M.	10 A.M.
Hemoglobin, gm.	15.8	12.8	Trans-	12.8	.....	11.0	10.2	11.6	.....
Red blood cells, millions	5	4.2	fusion,	4.08	.....	3.58	3.43	3.96	.....
White blood cells	10,400	12,900	500 cc.	28,800	.....	18,000	11,000	11,700	.....
Platelets	.....	20,000	whole	40,500	22,000	62,500	85,500	210,000	218,500
Bleeding time, min. (Duke)	.....	.....	blood	9	3½	2½	2½	1	.....
Heparin clotting time, min.	.....	.....	.....	22	20	22	21	18	.....
Serum prothrombin time, sec.	.....	.....	.....	29	17	45	32	.....	.....
Tourniquet test	.....	.....	.....	>300 petechiae	Negative	Negative	Negative	Negative	.....
Clot retraction	.....	.....	.....	All cut	Present	Present	Present	Present	.....

* Sternal marrow biopsy (Dr. Carl Reich) on Dec. 4 showed a granulocytic cell hyperplasia; megakaryocytes were diminished. On Dec. 10 the sternal marrow showed hyperplasia of all the elements.

† On Dec. 5, at 5 p.m., a transfusion of blood platelet concentrate (450 billion platelets) was given.

COMMENT

It is reasonable to assume that the thrombocytopenic purpura was induced by treatment with gantrisin.* Administration of a large number of platelets brought about prompt arrest of bleeding, and cessation of treatment with the drug permitted spontaneous regeneration of the bone marrow. The platelet count did not show an immediate rise, but this was to be expected since the platelets are probably withdrawn from the circulation as fast as they are administered, in the process of restoring a normal blood-clotting mechanism.

SUMMARY

A case of toxic thrombocytopenic purpura induced by treatment with gantrisin* (3,4-dimethyl-5-sulfanilamido-isoxazole) is reported. Recovery occurred with dramatic suddenness after cessation of treatment with the drug and a transfusion of blood platelets.

1070 Park Ave.

From the Achelis Laboratory, Lenox Hill Hospital.

1. Haunz, E. A.; Cardy, J. D., and Graham, C. M.: Agranulocytosis Due to Gantrisin®: Report of a Case with Recovery, J. A. M. A. **144**: 1179 (Dec. 2) 1950.

2. Hagerman, D. D., and Franzblau, S. A.: Gantrisin® (Sulfisoxazole)-Induced Granulocytopenia, J. A. M. A. **147**: 1657 (Dec. 22) 1951.

3. Gale, G. L.: Petechial Hemorrhages with the Use of Gantrisin (NU-445), Canad. M. A. J. **64**: 252 (March) 1951.

4. The platelet concentrate was prepared in the Laboratory of Experimental Cytology, Lenox Hill Hospital, by the method of Minor and Barnett (to be published).

COUNCIL ON PHARMACY AND CHEMISTRY

REPORT TO THE COUNCIL

Some months ago in a random sampling 50 physicians in California were asked the question, "If a narcotics addict came to you for treatment, what disposition would you make of the case?"

Inasmuch as four of the physicians queried indicated that they would treat the addict, while the others gave varied answers, the Council, believing that physicians in general would appreciate a discussion of the question, has authorized publication of the following statement. This statement has been prepared by the Committee on Drug Addiction and Narcotics of the National Research Council with the assistance of Dr. Harris Isbell, Director, National Institute of Mental Health Addiction Research Center, United States Public Health Service Hospital, Lexington, Kentucky.

R. T. STORMONT, M.D., *Secretary.*

WHAT TO DO WITH A DRUG ADDICT

A recent questionnaire circulated in southern California revealed that many physicians were uncertain as to the proper course to be taken when drug addicts appeared in their offices. This paper has been prepared to provide information on the proper procedure in this situation. It will deal only with addiction to those substances covered by the Harrison Narcotic Act and similar laws, such as the Marihuana Tax Act. Specifically, the drugs concerned are opium and all mixtures containing opium, morphine, heroin, dihydromorphinone (dilaudid®), methyldihydromorphinone (metopon), 3-hydroxy-N-methylmorphinan (dromoran®), codeine, dihydrocodeinone (hycodan®), dihydrohydroxycodeinone (eukodal), meperidine (demerol®), methadone (dolophine,® adanon®), marihuana, and cocaine.

PERTINENT FEDERAL REGULATIONS

All physicians who prescribe and dispense narcotics are furnished by the Bureau of Narcotics, U. S. Treasury Department, with Regulations No. 5 relating to the "dealing in, dispensing and giving away of opium or cocoa leaves, isonipecaine or opiates, or any compound, manufacture, salt, derivative or preparation thereof" and with Pamphlet No. 56, "Prescribing and Dispensing of Narcotics under the Harrison Narcotic Law." All physicians should be familiar with these two publications and, furthermore, should realize that the synthetic narcotics, meperidine, methadone, and dromoran,® have been legally defined as opiates and subjected to the same regulations as are morphine and its derivatives. The most pertinent statement concerning addiction is Article 167 of Regulations No. 5, which reads in part as follows: "An order purporting to be a prescription issued to an addict or habitual user of narcotics not in the course of professional treatment, but for the purpose of providing the user with narcotics sufficient to keep him comfortable by maintaining his customary use, is not a prescription within the meaning and intent of the act; and the person filling such an order, as well as the person issuing it, may be charged with violation of the law."

This regulation is interpreted in Pamphlet No. 56, which reads in part as follows: "The responsibility for the proper prescribing and dispensing of narcotic drugs under the Harrison Narcotic Law rests upon the physician in charge in any given case . . . [and] corresponding responsibility rests upon the druggist who fills the prescription to determine, in good faith, that the prescription was issued in the course of professional practice and not for the purpose of gratifying addiction . . . The good faith of the physician and the bona fides of his treatment in a given case will be established by the facts and circumstances of the case and the consensus of medical opinion with regard thereto, based upon the experience of the medical profession in cases of similar nature. Physicians will be expected to exercise such care in every case where narcotic usage is indicated, that the patient under treatment shall receive no quantity of narcotic drug greater than that sufficient for bona fide medical needs in order that there may be no surplus available for possible diversion by the patient to illicit use . . . Mere addiction alone is not regarded or recognized as an incurable disease. It is well established that the ordinary case of addiction yields to proper treatment and that addicts can remain permanently cured when drug taking is stopped and they are otherwise physically restored to health and strengthened in will power."

Many of the individual states have passed narcotic control laws and the physician must be familiar with the laws and regulations of his particular state as well as with the Federal laws. In general, the physician will be acting in accordance with the consensus of medical opinion with regard to addiction and will be complying with the letter and spirit of the regulations if he follows two principles: (1) Ambulatory treatment of addiction should not be attempted as institutional treatment is always required; (2) Narcotic drugs should never be given to an addict for self-administration.

The reasons for establishing these principles are set forth in a committee report adopted by the House of Delegates of the American Medical Association in 1924. The following are excerpts from this report: "Your committee desires to place on record its firm conviction that any method of treatment for narcotic drug addiction, whether private, institutional, official or governmental, which permits the addicted person to dose himself with the habit-forming narcotic drugs placed in his hands for self-administration, is an unsatisfactory treatment of addiction, begets deception, extends the abuse of habit-forming narcotic drugs and causes an increase in crime . . .

"In the opinion of your committee, the only proper and scientific method of treating narcotic drug addiction is under such conditions of control of both the addict and the drug that any administration of any habit-forming narcotic drug must be by, or under the direct personal authority of the physician with no chance of any distribution of the drug of addiction to others, or opportunity for the same person to procure any of the drug from any source other than from the physician directly responsible for the addict's treatment."

DIAGNOSIS OF ADDICTION

Most frequently, addicts who appear in a physician's office are transients who are unknown to the physician. Such persons are likely to appear when circuses and carnivals are present in a community. Less commonly, addicts may be nontransient persons who are fairly well known to the physician. Frequently, nontransient addicts are neurotic persons or are patients who are known to have been chronic alcoholics. It is not unusual for the nontransient addict to be a physician. In recent years, it has not been unusual in certain areas for an adolescent boy or girl to be brought to the physician by relatives or by representatives of social organizations for advice relative to the treatment of addiction.

Most frequently, the diagnosis of addiction is made at the onset of the interview by the patient's statement that he is addicted to and needs drugs. The addict may attempt to conceal his addiction and may present a glib story of some physical illness; most frequently mentioned are atypical angina pectoris, kidney colic, migraine, or hemorrhoids. Generally, the story culminates with the suggestion that other physicians have found that the only adequate remedy is a prescription for narcotic drugs. Frequently, addicts of this type may appear armed with a formula which they state was given to them by another physician and which they have found very effective for the relief of their alleged symptoms. The formula will usually contain morphine, laudanum, or cocaine. If refused morphine, many addicts will ask for either methadone or meperidine. They will state that these drugs are not opiates but are synthetic drugs and are nonaddicting. All too frequently, uninformed physicians will be taken in by this story and will prescribe the synthetic analgesics. It is not unusual for addicts to attempt to obtain narcotics on the basis of some mild, chronic, nonfatal disease, such as asthma, arthritis, or chronic osteomyelitis, for which narcotics are not usually required or given. They will state that these diseases cause them terrible pain, that physicians in another town have been prescribing narcotics, and that their own physicians are away and they need drugs only until he returns. Occasionally,

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transient addicts may appear who are suffering with serious physical diseases, such as advanced cardiovascular diseases or emphysema. These cases present particularly difficult problems of treatment since the stress of abrupt withdrawal might prove fatal.

Nontransient addicts who are well known to the physician sometimes attempt to develop stories similar to those used by the transient, veteran, criminal type of addict. Nontransient addicts, however, are more likely to be sincere than the transient addict. Many such patients truly desire to be cured of their addiction and should be given all possible help. All too frequently, a nontransient addict will be a physician or a nurse. In such cases, the most likely drug of addiction is now meperidine largely because of the widespread belief among the medical profession that this substance is not addicting.

The presenting situation may also be that of an adolescent girl or boy who is brought to the physician by his parents or by other responsible persons. Generally, such adolescents will admit the use of drugs and present no particular problem in diagnosis. In such cases, the physician should exercise a certain degree of care since, because of the widespread publicity concerning addiction in adolescents, many parents may wrongly attribute normal or abnormal adolescent behavior to drug addiction.

When the history leads one to suspect addiction, a complete physical examination is of the utmost importance. A transient addict is frequently surprised when the physician indicates a desire to perform a complete physical examination and may refuse the examination and immediately leave the office. It is important to realize that there are no pathognomonic physical signs of addiction. The opiate drugs do not cause drunkenness as do the barbiturates and alcohol, so mental confusion, emotional instability, nystagmus, and ataxia are not to be expected. Since complete or partial tolerance to many of the effects of morphine develops during the course of addiction, doctors must not expect that addicts presenting themselves in their offices will show the same effects as might be expected in persons not addicted, namely, constriction of the pupils and sedative effects. An addict may or may not show pupillary constriction depending on how recently he has received a dose of morphine. Superficially, tolerant addicts will appear to be physically and mentally normal unless they have been without drugs for some time and signs of abstinence have appeared.

The most important findings are the presence of old and recent needlemarks. These needlemarks should be sought over the veins in the antecubital spaces, the deltoid region, the abdomen, the anterior surface of the thighs, and along the veins of the legs and hands. Multiple abscesses or old abscess scars are also suggestive. Miosis is not a completely reliable sign since partial tolerance to pupillary constriction caused by morphine develops during addiction. Addicts who are using either meperidine or methadone are likely to have induration and inflammation of large areas of the skin, particularly over the deltoid region and the anterior surface of the thighs. Presence of long scars or tattooing over superficial veins is extremely suggestive, particularly if fresh needlemarks are present. One important feature may be that no physical findings are present which satisfactorily explain the serious symptoms detailed by the patient when the history was taken.

Occasionally, persons who are suspected of taking cocaine or marihuana are brought to the physician for an opinion. Neither cocaine nor marihuana produces physical dependence. Since such patients are usually brought to the physician long after the drug effects have worn off, findings are generally scanty. The signs of cocaine intoxication, however, include mydriasis, sweating, tachycardia, increase in blood pressure, increase of deep tendon reflexes, nervousness, tremor, an unblinking stare, and auditory and visual hallucinations. Intoxication with marihuana is characterized by injection of the conjunctivae, a sleepy appearance, excessive giggling, silly behavior, absence of marked ataxia, and a strong odor on the breath resembling that of cubeb cigarettes.

There are no laboratory procedures generally available to the average physician which are helpful in the diagnosis of addiction. Reliable tests for the presence of morphine and cocaine in the urine have been developed, but these methods are quite complex and are not suitable for use in the ordinary laboratory. There are no methods available for the detection of morphine in blood and no laboratory procedures which are sufficiently specific for the detection of synthetic analgesics and marihuana in either blood or urine. Furthermore, if such procedures were available, a positive test of the presence of drugs in the urine would mean only that the person had recently taken or been given a dose of a drug and would not necessarily mean that he was addicted to that drug.

A definitive diagnosis of addiction to morphine or similar drugs depends upon the demonstration of the characteristic signs of abstinence following complete and abrupt withdrawal of drugs. In order to prove the presence of physical dependence, the addict must be isolated in an environment so well controlled that there is no possibility of any narcotic drugs, other than those prescribed, being obtained by the addict. If such an environment is available, isolation of the addict and withholding of all narcotics will prove the presence or absence of dependence on these drugs. The detection of physical dependence requires familiarity with the signs of abstinence from morphine.

If morphine is abruptly withdrawn from a patient who has been receiving as much as 0.26 to 0.39 gm. (4 to 6 grains) daily for a period of 30 days or more, few signs are observed during the first 16 hours of abstinence. The patient is likely to go into a restless, tossing sleep which may last for several hours. About 14 to 18 hours after the last dose of the drug was given, the addict will begin to yawn; rhinorrhea, perspiration, and lacrimation will appear. These mild signs increase in intensity during the first 24 hours of abstinence; thereafter, they become constant. Dilatation of the pupils then appears and, on close observation, recurring waves of gooseflesh will be seen. About 36 hours after the last dose of morphine was given, uncontrollable twitching of the muscles occurs. The patient will become extremely restless, will move from side to side in bed, and tremor of the face and tongue will be evident. The patient will complain of severe cramps in his legs, abdomen, and back; he will be unable to eat or to sleep for any period of time and vomiting and diarrhea frequently occur. Rectal temperature rises about 2 F, respiratory rate is usually elevated to 20 to 30 per minute and is increased in depth. Systolic blood pressure is usually elevated about 15 mm. of mercury, and patients will lose 5 to 15 pounds of weight during the second 24 hours of abstinence. A reduction in eosinophils per cubic millimeter of blood closely parallels the intensity of abstinence symptoms, and, at the peak intensity of the withdrawal illness, the eosinophil count will be nearly zero. This constellation of signs and symptoms constitutes as clear-cut and well delineated a syndrome as is ever seen in clinical medicine. Once it has been observed, it scarcely can be mistaken for any other condition. Acute signs and symptoms reach maximum intensity 48 hours after the last dose of morphine has been given and will remain intense until 72 hours have passed. Thereafter, they gradually subside and, after 5 to 10 days, completely disappear, although the addict may still be weak and sleeping poorly.

It is necessary to remember that the intensity of the abstinence syndrome varies from person to person and is, within limits, dependent on the dose that the addict has been receiving. Not all patients will exhibit all the signs of abstinence listed above. Severe grades of abstinence symptoms are practically always seen in addicts who have been receiving as much as 60 to 90 mg. (1 to 1.5 grains) of morphine four or more times daily. The intensity of abstinence symptoms becomes milder as the average daily dose declines. Since most adolescent addicts actually have been receiving only small amounts of opiates, the effects of abstinence are usually quite mild in juvenile addicts and very close examination may be required to detect the minor signs which are present.

Symptoms of abstinence from other opiates and the synthetic analgesics differ from morphine chiefly in intensity and duration. Effects of abstinence from heroin, dihydromorphinone, and metopon appear very rapidly, reach maximum intensity in 12 hours or less, are somewhat more severe than those from morphine, and subside more rapidly. Abstinence symptoms from codeine appear slowly and are more prolonged than those from morphine. Abstinence symptoms from dihydrocodeinone and eukodal are less intense than those from morphine, but more intense than those from codeine. The symptoms from dromoran* are quite similar in course and intensity to those from morphine.

Effects of abstinence from meperidine appear rapidly and are detectable two to three hours after the last dose of meperidine has been administered. Abstinence from meperidine has an effect somewhat similar to that of abstinence from morphine, but restlessness is even greater, and uncontrollable twitching and jerking of the muscles is extreme. The course of abstinence from meperidine is quite short and symptoms usually disappear two to three days following withdrawal.

Signs of abstinence from methadone come on slowly and are usually not detectable until the third or fourth day after the last dose of the drug has been given. Autonomic signs, such as sweating and mydriasis, are not very prominent. For this reason, the detection of abstinence symptoms is more difficult. The course of abstinence from methadone, however, is quite prolonged. Because of this, withdrawal of methadone is regarded by many addicts as being more uncomfortable than abstinence from morphine.

Frequently, because of the lack of suitable facilities, it may not be possible to isolate the addict and prove the presence of addiction by allowing the signs of abstinence to appear. It is almost useless to attempt to carry out diagnostic withdrawal in a general hospital, or even in mental hospitals, since addicts frequently manage to smuggle drugs into these environments. Diagnostic withdrawal may also be impossible because of the addict's refusal to undergo the procedure and, in certain cases, it may be unwise if the patient has some serious physical disease.

Where adequate isolation for diagnostic withdrawal is not possible, the diagnosis of addiction can be established only tentatively.

A new drug, N-allylnormorphine, which is a very effective antidote for morphine, has recently been shown to precipitate signs of abstinence in addicted persons within 15 minutes following its administration. This agent, therefore, may provide a means of quickly establishing the presence and degree of physical dependence on opiate drugs, but sufficient information on the safety and reliability of the procedure is not available at this time to permit a recommendation for general use of N-allylnormorphine as a diagnostic agent in suspected addiction.

REPORTING OF ADDICTS

The physician is under no legal obligation to report cases of addiction to Federal officials. The Bureau of Narcotics, however, welcomes voluntary reporting of addicts by physicians.

DISPOSITION OF THE ADDICT

Once a tentative diagnosis of addiction has been made, the physician would be well advised to seek consultation for confirmation. The problem then becomes one of advising the addict in accordance with the two cardinal principles of treatment set forth above—institutional treatment is necessary, and drugs must not be given to the addict for self-administration. The addict must be advised to seek admission to an institution for treatment. If he will not accept this advice, the physician may ethically refuse to take any further action. If the patient indicates willingness to undergo institutional treatment, steps should be taken immediately to obtain admission to the nearest and most available institution. Frequently, this can be accomplished immediately by telephoning the institution selected. The physician should refuse to administer any narcotics unless the patient shows the utmost diligence in obtaining entrance into an institution. Such excuses as time for arranging business and personal affairs or preference for one institution over another should not be accepted as reasons for the administration of narcotics; nor should the presence of signs of abstinence be a valid reason for immediate administration of narcotics unless the patient has such serious physical disease that stress of abstinence might prove fatal.

The physician must be prepared to resist the demands of addicts for narcotics and must exercise great care and judgment in determining whether physical disease which requires the immediate administration of opiates is present. If a physician yields to the importunities of an addict and gives him morphine for mild asthma, his waiting room will soon be cluttered with other addicts, all of them complaining that they have asthma or some similar condition. Such a situation can lead only to embarrassment to the physician and, perhaps, to difficulties with the authorities.

When the patient has agreed to go to an institution and has presented satisfactory evidence that he has taken steps to obtain admission (mere statement of the addict is not sufficient evidence of this), the problem is then reduced to the immediate management of the patient. The second principle, drugs should not be given to the addict for self-administration, applies here. It may be possible to place the patient in a general hospital where narcotics can be administered under direct supervision while final arrangements for entrance to the specialized institution are being made. The physician, in any event, should not give the addict a prescription for narcotics but should administer personally such drugs as are appropriate for immediate need only. It may be emphasized that it is always wise to seek consultation with another physician relative to the diagnosis of addiction and/or the presence of serious physical disease. A special record of narcotics administered should be kept, and, as has been previously mentioned, temporary administration of drugs should not be extended beyond the minimum time absolutely necessary for arrangements for admission to an institution to be completed. When the addict leaves his home community, he should be accompanied to the institution, whenever possible, by some responsible person, preferably a physician or a nurse.

No absolute rule can be laid down for the amount of narcotics to be given during the time arrangements for admission to a proper institution are being made. However, no amount of narcotic should be used in excess of that necessary for the immediate need of the patient. Either morphine or methadone may be used since these two drugs will adequately control abstinence from any of the other narcotics. It is advisable to limit the initial dose to 16 mg. (¼ grain) of morphine or 10 mg. (⅙ grain) of methadone. It practically never should be necessary to exceed as a single dose 60 mg. (1 grain) of morphine or 30 mg. (½ grain) of methadone. Even in patients with very severe heart disease, there is little danger of abstinence from morphine causing death if the above dosage schedule is followed. The type of drug given and the dose should be unknown to the addict and all possible precautions should be taken to prevent the addict from obtaining narcotics from other sources.

THE ADOLESCENT ADDICT WITH OR WITHOUT DEMONSTRABLE DEPENDENCE ON NARCOTIC DRUGS

Despite their ages, adolescent addicts must be separated from their usual environments. Institutional treatment for adolescents with demonstrable dependence is just as necessary as for adult addicts and the same procedures should be followed. Adolescents without physical dependence might possibly be sent to a camp, farm, or some other environment where rehabilitative treatment may be attained rather than sent to institutions where contact with older, more hardened addicts is unavoidable.

PATIENTS WITH INCURABLE, FATAL, PAINFUL DISEASES

Persons in this class are usually patients who are dying with advanced carcinoma, tuberculosis, or some other chronic disease. The problem in such instances is completely different from those described above. The physician is properly concerned, primarily, with relieving suffering and, only secondarily, with the addiction. Federal and State narcotic laws were not designed to prevent narcotics from being prescribed in such cases. Proper, ethical medical practice, however, demands that certain principles be followed.

Physicians prescribing narcotics for such patients should personally be attending the patient. A diagnosis of a painful, incurable disease should be confirmed by consultation with another physician. All means of relieving pain other than prescription of narcotics should be exhausted. Such measures include the use of drugs other than narcotics, physical therapy, and surgical procedures designed to relieve pain. When administration of narcotics becomes necessary, the physician should initially use drugs of lesser potency, such as codeine. When use of more potent narcotics is required, they should be given in the smallest possible dose and the interval of administration should be as long as possible. Precautions should be taken to ensure that the amounts of narcotics prescribed are no greater than those actually required for the particular patient so that there will be no surplus for diversion to illicit use. Whenever possible, the drugs should be given orally rather than hypo-

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dermically. Drugs should not be given directly to the patient for self-administration. The status of the patient and his disease should be reviewed periodically to make certain that the diagnosis is correct and that definitive, curative therapy is not possible.

COCAINE AND MARIHUANA ADDICTS

Since physical dependence on these drugs does not develop and there is no withdrawal illness, the patient should simply be advised to seek treatment in a properly staffed institution. Hospitalization until admission to an institution can be obtained is not necessary or advisable.

CHOICE OF INSTITUTION

The choice of an institution depends upon the type of case, the financial situation of the patient, and other factors. Many private sanatoriums in the United States make a specialty of the treatment of narcotic drug addiction. Advice concerning these institutions can be obtained from local medical societies, the American Hospital Association, The American Psychiatric Association, or the American Medical Association. Alternatively, the physician may investigate the possibilities of having the patient admitted to a public, local, or state institution. Information concerning such institutions can be obtained by contacting local or state health departments. Lack of suitable local facilities remains one of the difficulties in the treatment of addiction. Physicians should support the establishment of such facilities in states in which no provision for addicts has yet been made. Where local facilities are not available, addicts can be referred to the two federal hospitals maintained by the U. S. Public Health Service at Lexington, Kentucky, and Fort Worth, Texas. Persons addicted to opiates, synthetic analgesics, cocaine, and marihuana are eligible for admission to these institutions. Patients who are addicted to alcohol, barbiturates, or bromides are not eligible for admission to these federal hospitals unless they are also addicted to morphine, synthetic analgesics, marihuana, or cocaine. If the patient is indigent, treatment is available without charge. If the patient has funds, he is required to pay $5.00 daily for his treatment. Addicts entering these institutions are asked to remain at least 135 days before being discharged. Ordinarily, there is no waiting list for male patients and admission can be arranged readily by writing or telephoning the Medical Officer in Charge of either hospital. Only the institution in Lexington has facilities for female patients, consequently, women usually must wait for a short time before they can be admitted.

THE NEED FOR COMPULSION

Unfortunately, many addicts will not go to an institution or remain there until treatment is completed unless compelled to do so by legal means. There is a great need for legislation in most of the states which would make it possible to commit addicts to institutions where they would be forced to remain until maximum benefit of treatment had been obtained. The Federal Bureau of Narcotics has drafted a text of such a proposed law and will distribute copies to interested persons on request. Legislation has also been proposed which would make it possible for the two U. S. Public Health Service Hospitals that treat addicts to accept and hold addicts committed under state laws. Passage of such laws deserves the support of all physicians.

TREATMENT FOLLOWING DISCHARGE FROM INSTITUTION

The follow-up treatment after the patient has been discharged from an institution is usually the weakest link in the overall treatment of addiction, and it is in this particular phase of the problem that the ordinary physician can make the greatest contribution. The physician should do what he can to assist the addict to find a job following discharge from an institution. He can attempt to make arrangements, utilizing such social agencies as are available, to separate the addict from the environment which played a role in engendering the addiction. He should encourage the former addict to participate in the activities of community groups, such as churches and clubs. The physician can advise the relatives of a former addict respecting environmental and familial factors which may be contributing to the patient's difficulties. He can also administer such forms of psychotherapy as he is qualified to carry out. When suitable facilities are available, intensive psychotherapy by a qualified psychiatrist is of great value provided the patient is willing to accept such treatment. The addict should remain under close supervision for at least two years following discharge from an institution. Although the tendency to relapse is very great in addiction, the physician should maintain an optimistic attitude even in the face of repeated recurrence and should continually encourage and support the addict.

MANAGEMENT OF DISEASE IN FORMER ADDICTS

When a person who formerly has been addicted to morphine become afflicted with a disease for which narcotics are usually prescribed (this situation usually develops when a surgical operation becomes necessary), he should be handled just as if he had never been addicted. Since the former addict has been withdrawn from narcotics and has lost his tolerance to them, narcotics should be prescribed in the same doses and at the same intervals as is customary with persons who have never been addicted. Larger doses are not required. Narcotics should never be given to the former addict for self-administration and use of narcotics should be discontinued as soon as possible. The addict should then be supervised closely for a month or so in order to avert relapse to uncontrolled use of drugs.

MANAGEMENT OF ADDICTS WHO HAVE RELAPSED

The management of patients who have relapsed to abusive use of narcotic drugs should follow the same lines as detailed above. The only difference is that the period of supervision following discharge from an institution should be extended.

NEW AND NONOFFICIAL REMEDIES

The following additional articles have been accepted as conforming to the rules of the Council on Pharmacy and Chemistry of the American Medical Association for admission to New and Nonofficial Remedies. A copy of the rules on which the Council bases its action will be sent on application.

R. T. STORMONT, M.D., *Secretary.*

Aurothioglucose (See New and Nonofficial Remedies 1952, p. 441).

Schering Corporation, Bloomfield, N. J.

Suspension Solganal in Oil: 1.5 cc. ampuls. A suspension in sesame oil containing 6.7 mg., 16.7 mg., or 33.3 mg. of aurothioglucose in each cubic centimeter with 2% aluminum monostearate. Preserved with 0.1% propylparaben.

10 cc. vials. A suspension in sesame oil containing 10 mg., 50 mg., or 100 mg. of aurothioglucose in each cubic centimeter with 2% aluminum monostearate. Preserved with 0.1% propylparaben. U. S. Trademark 261,372.

Gamma Benzene Hexachloride (See New and Nonofficial Remedies 1952, p. 74).

Commercial Solvents Corporation, New York

Lotion Kwell 1%: 60 cc. and 500 cc. bottles. A lotion containing 10 mg. of gamma benzene hexachloride in each cubic centimeter.

Bismuth Glycolylarsanilate (See New and Nonofficial Remedies 1952, p. 145).

Winthrop-Stearns, Inc., New York

Tablets Milibis: 0.5 gm. U. S. Patent 1,934,017.

Penicillin for Injection for Prolonged Action (See New and Nonofficial Remedies 1952, p. 126).

Merck & Company, Inc., Rahway, N. J.

Procaine Penicillin G for Aqueous Injection: 300,000, 1,500,000, and 3,000,000 unit vials. Buffered with sodium citrate.

Human Pertussis Immune Serum-N.F. (See New and Nonofficial Remedies 1952, p. 380).

Junior League Blood Center of Milwaukee, Inc., Milwaukee

Pertussis Immune Serum (Human): 10 cc. and 20 cc. vials.

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CAUTION IN THE CHEMOTHERAPY OF TUBERCULOSIS

Three recently developed antituberculosis drugs, isoniazid (isonicotinic acid hydrazide), iproniazid (1-isonicotinyl-2-isopropyl hydrazine), and pyrazinamide, are now undergoing extensive clinical testing. These drugs have shown definite but limited therapeutic activity against human tuberculosis,[1] but there is much concern among workers in this field that their potential value may rapidly be neutralized if they are used improperly or indiscriminately by those not trained in the treatment of tuberculosis. The recent increase in the availability of isoniazid has brought this problem into acute focus.

One of the major threats to the effective use of the newer forms of tuberculosis chemotherapy lies in the possibility that physicians will attempt to use these drugs as the sole form of therapy. As the American Trudeau Society,[2] the American College of Chest Physicians,[3] and other organizations dealing with tuberculosis have repeatedly emphasized, these compounds are not in themselves cures in spite of the earlier optimistic publicity given to some of them. They, like other forms of chemotherapy, must be used as adjuncts to the time-tested measures of bed rest, collapse therapy, and surgical procedures. Moreover, as adjuncts they have not yet proved clinically superior to, or even so effective as, the combination of streptomycin and *p*-aminosalicylic acid in the treatment of tuberculosis.[2]

Another threat to the continued effectiveness of these drugs arises from the fact, now well established, that the tubercle bacillus is capable of developing resistance to them rapidly both in vitro and in vivo. In the clinic, bacilli resistant to isoniazid, iproniazid [4] and pyrazinamide [1b] have appeared in some cases after only two to four weeks of therapy, although a somewhat longer period is usually required. Such organisms seem to develop especially rapidly in patients with far-advanced cavitary pulmonary tuberculosis, and their appearance is associated with a recurrence of symptoms despite continued treatment. In the laboratory, bacilli with a 5-fold increase in resistance to iproniazid [5] and a 16-fold to 4,000-fold increase in resistance to isoniazid [6] have been obtained by serial passage on media containing these drugs. Resistance to isoniazid, like that to streptomycin, may develop in a single step [7] and may be present in organisms never previously exposed to the drug.[8]

These observations emphasize the need for care in the use of the new drugs. Steenken and co-workers,[9] and Grace and associates (see this issue, page 1241) warn that if these compounds are used alone they may benefit the patient only temporarily and may prejudice his chance of future response to combined drug therapy, surgery, or both. This practice may also result in the widespread appearance of strains of tubercle bacilli resistant to these drugs and in the eventual infection of others with organisms resistant to both streptomycin and isoniazid or one of the other compounds. It is suggested by Grace and associates that these drugs be employed only in multiple combinations with streptomycin and *p*-aminosalicylic acid or other chemotherapeutic agents active against mycobacteria and not related by cross resistance. They base this suggestion on the well-established fact that the production of resistant variants of an organism can be inhibited by simultaneous (but not consecutive) exposure of that organism to at least two drugs with different modes of action. That this general principle applies specifically to isoniazid is suggested by the observation that no tubercle bacilli resistant to either isoniazid or streptomycin have been encountered in cultures exposed simultaneously to therapeutic concentrations of the two drugs,[10] although strains resistant to both have been obtained by successive exposure to these compounds.[7b]

Still another hazard in the use of these drugs is that of inadequate dosage. Since there has not yet been time for adequate long-term evaluation of different dosage schedules for the different forms and stages of tuberculosis, it is obvious that no statement about optimum dosage

1. (*a*) New Antituberculosis Drugs, editorial, J. A. M. A. **148**: 1034 (March 22) 1952. (*b*) Yeager, R. L.; Munroe, W. G. C., and Dessau, F. I.: Pyrazinamide (Aldinamide) in the Treatment of Pulmonary Tuberculosis, Am. Rev. Tuberc. **65**: 523 (May) 1952.

2. Committee on Therapy of American Trudeau Society: Developments in Antimicrobial Therapy of Tuberculosis, May 26, 1952, Am. Rev. Tuberc. To be published.

3. Committee on Chemotherapy and Antibiotics of the American College of Chest Physicians: Isoniazid (Isonicotinic Acid Hydrazide), read at the meeting of the American College of Chest Physicians, Chicago June 5, 1952.

4. Steenken, W., Jr.; Meade, G. M.; Wolinsky, E., and Coates, E. O., Jr.: Demonstration of Increased Drug Resistance of Tubercle Bacilli from Patients Treated with Hydrazines of Isonicotinic Acid, Am. Rev. Tuberc. **65**: 754 (June) 1952.

5. Steenken, W., Jr., and Wolinsky, E.: Antituberculous Properties of Hydrazines of Isonicotinic Acid (Rimifon, Marsilid), Am. Rev. Tuberc. **65**: 365 (April) 1952.

6. (*a*) Buck, M., and Schnitzer, R. J.: The Development of Drug Resistance of M. Tuberculosis to Isonicotinic Acid Hydrazide, Am. Rev. Tuberc. **65**: 759 (June) 1952. (*b*) Karlson, A. G., and Ikemi, Y.: The Occurrence of Human-Type Tubercle Bacilli (H37Rv) Resistant to Isonicotinic Acid Hydrazide in a Culture Not Previously Exposed to the Drug, Proc. Staff Meet., Mayo Clin. **27**: 239 (June 4) 1952.

7. (*a*) Pansy, F.; Stander, H., and Donovick, R.: In Vitro Studies on Isonicotinic Acid Hydrazide, Am. Rev. Tuberc. **65**: 761 (June) 1952. (*b*) Szybalski, W., and Bryson, V.: Bacterial Resistance Studies with Derivatives of Isonicotinic Acid, Am. Rev. Tuberc. **65**: 768 (June) 1952.

8. Hobby, G. L., and Lenert, T. F.: Resistance to Isonicotinic Acid Hydrazide, Am. Rev. Tuberc. **65**: 771 (June) 1952. Karlson and Ikemi.[6b]

9. Steenken, W., Jr.; Meade, G. M.; Wolinsky, E., and Coates, E. O., Jr.: Drug Resistant Tubercle Bacilli from Patients Treated with Isonicotinic Acid Hydrazides, correspondence, J. A. M. A. **149**: 187 (May 10) 1952.

10. Middlebrook, G.: Sterilization of Tubercle Bacilli by Isonicotinic Acid Hydrazide and the Incidence of Variants Resistant to the Drug in Vitro, Am. Rev. Tuberc. **65**: 765 (June) 1952. Pansy, Stander, and Donovick.[7a]

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or duration of administration can be made. It should be equally obvious that, until such information is available, use of the drugs should be limited to institutions where rigidly controlled observations on different treatment schedules can be made, recorded, and pooled with those of other institutions for final evaluation. Random use of the drugs on an empirical basis can result only in waste, inefficiency, inconclusive results, and harm to some patients.

While there have been few toxic reactions to these drugs to date with the doses used, such reactions must be watched for carefully during and after therapy. According to the Committee on Therapy of the American Trudeau Society, "isolated instances of intractable asthma, persistent hypotension, and increased susceptibility to the effects of other drugs (particularly epinephrine, ephedrine, atropine, and demerol) and even deaths have been reported in patients receiving isoniazid or its isopropyl derivative, but the causal relationship has not been clearly established. Minor untoward effects which have been reported are hyperreflexia, constipation, postural hypotension and dizziness, difficulty in starting micturition, eosinophilia, and the appearance of casts, albumin, and reducing substances in the urine. Routine precautions during treatment should include frequent neurologic examinations, blood counts, urinalyses, and tests for renal and hepatic insufficiency. As both drugs are excreted through the kidneys, impairment of renal function may result in the cumulation of toxic concentrations of the drug in the body. For this reason, the renal function should be measured before treatment and, if it is impaired, the dose should be reduced accordingly." [2]

These facts must be considered carefully by every physician contemplating the use of one of the new drugs in a patient with tuberculosis.

FULL COST TUITION IN MEDICAL SCHOOLS

One of the remedies that has been suggested for the present financial problems that confront the medical schools is that the schools charge their students for the full cost of their education. This suggestion usually is advanced by those not close to medical education, but it has received at least passing attention by a few schools in recent years. Fortunately, the great majority of medical schools have been quick to see the dangers of such a program and have refused to give it serious consideration.

Elsewhere in this issue, page 1243, the Council on Medical Education and Hospitals has an important statement summarizing the many damaging effects that could result from attempts to charge medical students for the full cost of their education. The Council points out that a plan of charging full cost tuition differs only in technical details from the practices of the proprietary medical schools at the beginning of the present century. The Council further gives several reasons why such a program would probably give only temporary relief and in time would actually make the situation of the medical schools worse. It is predicted that such a program would soon discourage support of the medical schools by other sources that have been so carefully cultivated and to whose interest and support much of the present excellence of our medical schools is due.

The school adopting such a program would itself soon suffer greatly. It would be at a serious disadvantage in the competition for able students and would probably find itself largely a school of last choice.

The Council properly fears that the consequences to the ideals and ethics of medical practice that might result from such a plan would be one of its most disastrous features. If medical education is placed on a dollar for dollar basis, the graduate laboring under a large debt could easily be tempted to regard his practice as a business enterprise purchased in the market place to be exploited and commercialized accordingly. Because of these and other inherent and potential dangers, the Council very rightly concludes its statement by condemning plans for charging full cost tuition and by urging the medical schools to continue to cultivate and expand accepted sources of support.

CLOTHING PROTECTION AGAINST RADIATION HAZARDS

In his endless struggle to protect himself against the demands of an exacting environment, man has successfully utilized various types of protective clothing to oppose the destructive action of fire, water, and noxious chemicals. Recently, Holden and Owings [1] called attention to the role of protective clothing in reducing some of the hazards of atomic and radiological warfare. Although clothing does not afford protection against the high neutron and gamma fluxes from an atomic bomb blast, it can protect against alpha, beta, infra-red, and ultraviolet radiations. Following an atomic explosion, an area of variable size is quickly contaminated by radioisotopes emitting alpha, beta, gamma, and x-radiations; in contrast, the hazard found in radiological warfare is due principally to a single type of radiation.

Alpha radiation emanating from an area contaminated by an atomic bomb burst causes damage when it affects the body internally. Effective protection against external contact with alpha radiation is made possible by wearing thin clothing. Ordinarily clothing will reduce a beta-ray flux from combined fission products, but shielding against gamma radiation by means of wearing apparel is impractical today. Since radiation produced by an atomic blast includes beta and gamma rays, this circumstance is analogous to one in which a warrior wearing medieval armor is exposed simultaneously and equally to a combined discharge of arrows and bullets. The armor provides full protection against arrows but incomplete protection against bullets. Similarly, clothing protects adequately against beta rays but inadequately against gamma radiation. All types of radioisotopes are fraught

1. Holden, F. R., and Owings, A. F.: Protection Afforded by Clothing Against Radiation Hazards, A. M. A. Arch. Indust. Hyg. 6:67 (July) 1952.

with peril when inhaled or ingested, alpha rays being more damaging locally to internal body structures than beta rays or gamma rays, and beta rays more destructive than gamma rays. Ingestion is due to the transference of radioactive materials from clothing to the mouth via the hands.

While clothing provides limited protection against external radiation, the controlled use of clothing serves not only to lessen body contamination and reduce the dangers of ingestion and inhalation but also to prevent the spread of radiocontaminants. There are numerous instances in which radioactive substances have been transported into previously uncontaminated areas by shoes. The spread of radioisotopes is the atomic age counterpart of Typhoid Mary.

In conclusion, it may be pointed out that the value of protective clothing in atomic and radiological warfare lies in the control of contamination rather than in providing protection against external radiation. The civilian population should be taught to care for itself when trained personnel and decontamination centers are not available. The basic requirements of a decontamination center are laundry facilities, monitoring instruments, and showers that have segregated clean and contaminated areas on either side of them. As for clothing itself, wearing apparel should be light in weight, nonporous, washable or expendable, and should completely cover the body, especially at the wrists, ankles, and the neck. Finally, light-colored clothing reflects infra-red radiation, thereby minimizing burns.

SURVEY OF DISCHARGED MEDICAL PERSONNEL

An increasing number of physicians are being discharged each month from military service after completion of their statutory tour of duty. In some instances dissatisfaction has been expressed with the utilization of medical personnel by the armed forces and the type of duties assigned. In an effort to evaluate the validity of the complaints, the Council on National Emergency Medical Service is contacting all physicians discharged from service since July 1, 1951. The questionnaire being distributed is designed to determine the use made of physicians by the armed services, the amount of time spent on the treatment of other than military personnel, and ways in which the American Medical Association can better serve medical personnel in uniform.

In addition to providing a service to physicians on active duty and those about to enter the armed services, it is hoped that the results of the survey will provide a sound basis for recommendations concerning the "doctor draft law." This law, which was originally enacted on Sept. 9, 1950, with the approval of the American Medical Association, was designed to supply physicians for the armed services. Inasmuch as this act will expire on July 1, 1953, it is necessary to establish a position as to whether legislation of this type should be extended and, if so, the form that it should take.

It is the earnest desire of the American Medical Association to apprize itself of the facts in this regard, to attempt to correct any justifiable source of complaint, and to formulate sound and constructive recommendations with respect to future draft legislation.

SAMPLE OF 1951 PHYSICIANS' INCOMES

On Wednesday of this week the Office of Business Economics of the U. S. Department of Commerce published the results of its interim professional income surveys for physicians, dentists, and lawyers. Unlike the bench mark study of 1949, which involved the analysis of 30,000 replies, the current survey of physicians' incomes is based on less than 1,000 replies from a sample of approximately 5,000 physicians selected by the Bureau of Medical Economic Research of the American Medical Association. The mean net incomes for 1950 and 1951 were $11,538 and $12,518 as compared with $11,058 reported in the big survey of 1949 income.[1]

The key sentence in the report of the 1949 survey published in the Survey of Current Business [2] was: "During the same period [1929-1949], all earners in the general population (wage and salary workers, as well as independent business and professional workers) recorded almost the identical relative increase (109 as compared with 108 percent) as all physicians." The same relationship held in 1950 and 1951 according to the results of this small sample; that is, the average net incomes of physicians are just keeping pace with the rise in the incomes of all earners in the general population. The incomes of the physician and the patient continue to grow apace.

THE NEW KEOGH-REED BILLS

Elsewhere in this issue (page 1244) is an explanation of the new features of the revised Keogh-Reed bills to establish a voluntary pension system. This revised version was introduced in the House of Representatives on June 27, too late to be considered in the closing days of the session. The bills as revised incorporate all the amendments suggested by the American Medical Association. Physicians should acquaint themselves with the provisions of the revised bills so that they can discuss these (identical) bills with other self-employed persons and pensionless employed persons such as lawyers, dentists, farmers, retailers, when they are asked for their opinions. They may also be asked for an opinion by their local candidates for the House and the Senate, as this measure is important to professional men and women.

1. Dickinson, F. G., and Bradley, C. E.: Survey of Physicians' Incomes, J. A. M. A. **146:** 1249-1255 (July 28) 1951. Reprinted as Bulletin 84, Bureau of Medical Economic Research, American Medical Association, Chicago, 1951.

2. Weinfeld, W.: Income of Physicians, 1929-49, Survey of Current Business, (July) 1951, U. S. Department of Commerce.

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THE PRESIDENT'S PAGE

A MONTHLY MESSAGE

In going about the country, I have become increasingly convinced that the general public and our own members still need to know more about the American Medical Association and its activities. In certain areas it is regarded by the public as a pressure organization devoted to the interests of management and industry and its own selfish interests. It has the reputation of being undemocratic. Its own members are often too little aware of the vast amount of work done by the Association in education, public health, and in eliminating fraud and charlatanism. The public in many cases believes that the Association limits the number of doctors and is against the socialization of medicine only for pecuniary reasons.

This is a shocking situation, and our public relations must continue to educate both the profession and the public as to the actual facts and must disabuse their minds of all these impressions, none of which are based on fact. In this and succeeding President's pages, I plan to further outline the real status and policies of the Association.

First of all, let us follow an idea that has germinated in the mind of an individual member. This member desires to see the A. M. A. adopt a certain policy that he has outlined in a resolution. There are two courses he can follow. First, he may take the resolution to his county society and introduce it there. He may present his arguments in open meeting, where he can be asked questions. A debate follows. If it is a good idea, his county society may approve the resolution and send it to the state society house of delegates with instructions to the county society delegates to introduce it. It may also circularize other county societies and enlist their support.

This resolution then is introduced into the house of delegates of the state, where it is immediately referred to a reference committee. The proponents of the resolution then appear before the reference committee and argue their case. One does not have to be a member of the house to appear before a reference committee and be heard. The reference committee then accepts, amends, or rejects the resolution and reports to the house. Final action is determined by the house. Again, if it meets with the approval of the majority of the house, it is forwarded to the A. M. A. House of Delegates, where the state's delegates are instructed to introduce it and work for its passage. Again, this may be circulated to other states before the meeting.

In the A. M. A. House of Delegates the same procedure is followed. Again, any member of the A. M. A., whether or not a member of the House, may appear before the Reference Committee and argue on the merits or demerits of the resolution. If the majority of the House concurs, the resolution becomes a part of the policies of the A. M. A. and the Board of Trustees is directed to carry out the policy. A single member, therefore, who holds no office or official position in any body can follow his idea right to the top. What could be more democratic?

Another method that can be followed is for the individual member to ask a member of the House to introduce the resolution direct, where it will follow the usual procedure. I followed this method once, myself. Twenty-three years ago, when I was in the government service, I desired the support of the A. M. A. in a method that was being pursued in the physical selection of airplane pilots. I asked a member of the A. M. A. House to introduce the resolution. I convinced him that approval of it was desirable. He introduced it, and both he and I appeared before the Reference Committee to support it. He was known by the Committee, but I was not, and I did most of the talking and answered most of the questions. I could not have received more courteous attention had I been President of the A. M. A. instead of a completely unknown member. The Reference Committee brought in a favorable report, and the House adopted the Resolution unanimously. Do you know of any other organization in which the individual member has more democratic rights?

Next month I expect to continue this discussion of the A. M. A., its policies, and its relation to the public.

LOUIS H. BAUER, M.D., HEMPSTEAD, N. Y.

ORGANIZATION SECTION

FEDERAL COMMUNICATIONS COMMISSION POSTPONES EFFECTIVE DATE FOR REPLACEMENT OF DIATHERMY EQUIPMENT

The effective date for compliance with the rules of the Federal Communications Commission has been postponed for one year. Physicians or hospitals now using nonconforming short wave diathermy apparatus have until June 30, 1953, to replace the diathermy equipment that does not conform with the rules of the Federal Communications Commission.

The Council on Physical Medicine and Rehabilitation forwarded a petition to the Federal Communications Commission on March 14, 1952, requesting an extension of the final date for one and one-half years. The following reasons were given for an extension. 1. Several thousand physicians and hospitals would be in violation of the rules of the commission or would have to deprive their patients of the therapeutic benefits of diathermy apparatus. 2. The present capacity of the industry to produce ample diathermy appliances was insufficient owing to cut-backs of materials and difficulty in obtaining labor. The Council was supported by several medical and industrial organizations in its request for an extension of time.

In Public Notice 77631, dated June 26, 1952, the Federal Communications Commission announced the extension of the effective date to June 30, 1953. In extending the date the commission pointed out that any further requests for extension of time would be subject to special investigation of individual cases. The commission pointed out the importance of physicians and hospitals equipping themselves with conforming diathermy equipment.

Requests have come to the Council on Physical Medicine and Rehabilitation concerning the possibility of converting short wave diathermy apparatus to conform with the rules of the F. C. C. The Council has been informed by reliable agencies that this is a difficult electrical and mechanical procedure and that the costs involved were as much, if not more, than replacing the equipment with council-accepted and the F. C. C.-approved type of short wave diathermy apparatus. The reconversion of diathermy equipment must be certified by reliable engineers. Surgical diathermy equipment for the generation of electric cutting currents, electric desiccation, and electric coagulation, used only for these medical purposes, are exempt and do not have to be replaced.

HANDBOOK FOR DOCTORS' SECRETARIES

An attractive booklet entitled "Winning Ways with Patients" is the newest A. M. A. public relations aid for physicians. It is a public relations handbook for the physician's secretary, receptionist, or medical assistant, designed to teach medical personnel how to make every patient's contact with the physician or his office staff as pleasant and satisfying as possible.

Because many patients complain "the doctor keeps me waiting too long," one section of the booklet is devoted to techniques for scheduling appointments, fitting patients without appointments and referred patients into the schedule, and keeping patients happy while they are in the waiting room.

Brightly illustrated, "Winning Ways with Patients" discusses telephone techniques, the best methods of billing and collecting medical fees, and other suggestions for improving doctor-patient and secretary-patient relationships. Personality traits, proper office dress, the importance of keeping office confidences, and the various responsibilities of the doctor's assistant are stressed.

This booklet, prepared by the Public Relations Department of the American Medical Association, will be mailed to all physicians in the United States after Aug. 1, and will also be made available to medical societies sponsoring courses for medical secretaries and assistants.

A. M. A. TO SPONSOR PUBLIC RELATIONS INSTITUTE

The American Medical Association's first Public Relations Institute will be held Sept. 4-5 at Chicago's Edgewater Beach Hotel. Featuring clinics covering a variety of practical PR problems, the institute will stress "Putting PR to Work" in local medical society programs. Subjects to be discussed at the two day meeting include increasing member-participation, developing better press-radio-TV relations, working with community groups, strengthening public service activities, carrying on field service activities, editing a society newsletter, utilizing direct mail techniques, and planning radio and TV programs.

Designed primarily for lay public relations personnel of state and county medical societies, the institute will supplement the annual Medical Public Relations Conference to be held Dec. 1, prior to the A. M. A.'s Clinical Session in Denver.

STATE MEDICAL LEGISLATION

Louisiana

Bills Enacted.—H. 219, has become Act No. 202 of the Acts of 1952. It amends and re-enacts the law relating to depositions and discovery by providing, among other things, that in an action in which the mental or physical condition of a party is in controversy, the court in which the act is pending or in which the judgment was originally rendered may order him to submit to a **physical or mental examination by a physician.** The order may be made only on motion for good cause shown and upon notice to the party to be examined and to all other parties and shall specify the time, place, manner, condition, and scope of the examination and the person or persons by whom it is to be made. Reports of such examination shall be delivered to the person examined, or the results of the examination may not be used as evidence at the trial. H. 428 has become Act No. 150 of the Acts of 1952. It provides, among other things, that no body shall be **cremated** except upon the permit or approval of the coroner. H. 429, has become Act No. 151 of the Acts of 1952. It provides, among other things, that by mutual agreement between two-thirds of the coroners of any parish included in any congressional district of the state approved by the police jury of the parish in which such coroner has agreed, there may be established a **forensic laboratory** for the mutual use and benefit of such coroners which shall be at the disposal of the coroners and law enforcement officers of the parish. It also provides that following an autopsy, the coroner may retain any specimens or organs of the deceased which in his discretion are desirable or needful for anatomic, bacteriologic, chemical, or toxicological examination as well as for possible evidence before a grand jury or court. H. 864, has become Act No. 373 of the Acts of 1952. It places all nursing homes under jurisdiction of the state department of health and directs the department of health to provide rules and regulations governing the operation of such homes. It also makes it unlawful for anyone operating a nursing home to administer, **without a doctor's prescription,** any **sleeping potion or medicine or give hypodermic injections** to any inmate of such nursing home. S. 165, has become Act No. 288 of the Acts of 1952. It authorizes charity hospitals of the state to accept as patients persons suffering from **alcoholism.** S. 194, has become Act No. 296 of the Acts of 1952. It puts on a prescription basis the sale and distribution of **barbiturates** and other hypnotic and somnifacient drugs and also **central nervous system stimulants** such as amphetamine and desoxyephedrine. S. 279, has become Act No. 297 of the Acts of 1952. It provides that at least five members of the **state board of health** shall be duly qualified and registered physicians.

Massachusetts

Bills Introduced.—H. 2510, (Appendix E) and H. 2558, propose the creation and **establishment of a state school of medicine** and a state school of dentistry in the City of Boston or vicinity.

Bills Enacted.—H. 2525, Appendix B, has become Resolve No. 84 of the Laws of 1952. It provides for the continuation of a special commission for the purpose of continuing its investigation and study relative to **high blood pressure** and the problem of its control. S. 209, has become Chapter 535 of the Laws of 1952. It authorizes the department of mental health, in connection with the adjudication of restoration of soundness of mind to appoint two physicians certified by the **American Board of Neurology and Psychiatry,** Incorporated, to examine the subject and advise the court of his present mental condition.

Prepared by the Bureau of Legal Medicine and Legislation.

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MEDICAL NEWS

CONNECTICUT

Fluoridation of Water Supplies.—The joint conference committee of the Connecticut State Medical Society and the Connecticut State Dental Association has endorsed fluoridation of public water supplies to aid in the control of tooth decay and will recommend to its parent organizations that an educational program be developed to further acquaint the public and community leaders with the benefits of fluoridation. The Connecticut Health League, an organization of 25 state and voluntary health agencies, endorsed water supply fluoridation during its semiannual meeting June 20 at the University of Connecticut, Storrs. Two communities in the state, New Britain and Cromwell, already are fluoridating their water supplies.

Emergency Medical Services.—According to Dr. Edward J. Whalen, Hartford, president of the Connecticut State Medical Society, emergency medical services are now being sponsored by medical associations for more than 1 million Connecticut residents, half the state population. These 24 hour telephone emergency systems are operating in 12 principal communities and are part of a long-range community service program sponsored by the society and its eight component county medical associations. Cities of more than 50,000 population that now have medical association emergency systems in operation include Hartford, New Britain, Waterbury, Bridgeport, and Stamford. Smaller communities where the new systems are operating are Torrington, Danbury, Greenwich, Norwalk, Manchester, Norwich, and Putnam. In addition to the new telephone emergency plan, there are plans mutually arranged between physicians and local hospitals by which patients may obtain emergency medical attention. These plans have proved a valuable service in communities where facilities are inadequate for operation of the emergency telephone systems. The three principal requirements of the new plans are (1) that the system be sponsored and supervised by a medical group or association, (2) that emergency services be available at all times through a central telephone number, and (3) that an organized panel of physicians be available for emergency calls.

ILLINOIS

Dr. Geen Honored.—Dr. James S. Geen of Utica, who has practiced medicine for 50 years and has been a member of the board of the LaSalle County Tuberculosis Sanatorium for 30 years, was honored at a banquet, May 27, in Ottawa. Dr. Geen, who was named to the board of trustees three years after the sanatorium was opened, has served continuously since that time by appointment of the county board of supervisors. He is now president of the board of directors.

State Hospital Needs Help.—The Illinois Department of Public Welfare has issued a call for 153 medical workers to augment the staff of Chicago State Hospital. According to Mr. Fred K. Hoehler, department director, the institution needs 119 attendants, 14 physicians, 3 supervising nurses, 6 psychiatrists, 4 fellows in psychiatry, 1 bacteriologist, 2 dietitians, 1 hydrotherapist, and 3 senior medical students to help in the care and treatment of more than 5,000 patients. The positions are under civil service.

Chicago

Dr. Dragstedt Named Thomas D. Jones Professor.—Dr. Lester R. Dragstedt, chairman of the department of surgery of the University of Chicago Medical Center since 1947, has been named the Thomas D. Jones Distinguished Service Professor of Surgery, to succeed the late Dr. Dallas B. Phemister.

Dr. Dragstedt served as the Nathan Smith Davis professor of physiology and pharmacology and chairman of the department at Northwestern University from 1923 to 1925, when he was appointed to the surgery staff of the University of Chicago. Dr. Dragstedt received the gold medal of the American Medical Association in 1950, the silver medal of the Association in 1947, and the gold medal of the Chicago Medical Society for his work on gastric ulcer.

Cancer Incidence in Chicago Area.—A study of cancer incidence among residents of the Chicago area showed no real change from 1937 to 1947, according to a survey just released by the National Cancer Institute. The study showed a numerical increase, but that was attributed to the aging of the population. The survey results differ from those obtained in five previously published studies, dealing with the metropolitan areas of Atlanta, Denver, New Orleans, Pittsburgh, and San Francisco, where more significant increases in cancer incidence were noted. Dr. John R. Heller, National Cancer Institute director, said, "At present we can only speculate on the meaning of the 'no change' report for the Chicago area. It may, in part, denote geographical differences in cancer incidence. On the other hand, the differences in cancer incidence between Chicago and the other cities may be due in part to improved case-finding and diagnostic techniques. In Chicago there is some indication that diagnostic techniques were already at a fairly high level in 1937."

In the Chicago area, cancer occurs 100 times as often in persons over 65 as in children under 15; however, certain cancers were found to be relatively common in younger persons, notably the leukemias and lymphomas, and soft tissue, bone, and brain tumors. In women, the commonest cancers are those of the breasts, 25%; genital organs, 23%; and digestive system, 27%. In men, 40% of all cancers originate in the digestive system, 13% in the respiratory system, 10% in the genital organs, 8% on the skin, and 8% in the urinary tract. In cancer of the uterus, diagnosed in its early, localized stage, 90% of the patients were found to survive for a year. The survival rate drops to 71% when diagnosis is made after regional involvement, and to 35% when diagnosis follows metastasis. Further, the Chicago data indicate that cancer of the uterus, which is an easily accessible site, is discovered in a localized stage in only 54 of 100 cases. Here, then, is a great need for earlier diagnosis, the report finds. The study also notes that uterine cancer occurs 58% oftener in nonwhite women than in white women. This may be related to the number of pregnancies or the medical care received by mothers during childbirth. The Chicago survey was carried out through the Public Health Service with the cooperation of the Cook County Medical Society, the Chicago Hospital Council, and city and state health departments.

LOUISIANA

Advancement in Rank at Tulane.—Twenty-three advancements in rank among Tulane University's school of medicine faculty have been announced. Faculty members advanced to full professorships include John Adriani (surgery), Paul C. Beaver, Ph.D., (parasitology), Frederick F. Boyce (clinical surgery), Manuel M. Garcia (clinical radiology), Chapman G. Johnson (clinical obstetrics and gynecology), Otto Schales, D.Sc., (biochemistry), Walter S. Wilde, Ph.D., (physiology), and Willard R. Wirth (clinical medicine). New medical associate professorships were granted to Clarence T. Ray (medicine), Isidore L. Robbins (clinical medicine), John R. Snavely (medicine), and Alan G. C. White, Ph.D., (biochemistry). Raised to the rank of assistant professors were Elaine Louise Allen (clinical pediatrics), Jack R. Anderson (clinical otolaryngology), Roger B. Bost (clinical pediatrics), Louis S. Charbonnet (clinical surgery), John K. Hampton Jr., B.S., (physiology), Lee C. Schlesinger (clinical orthopedics), Charles C. Sprague (medicine), Harold G. Tabb (clinical otolaryngology), Walter G. Unglaub (medicine), Richard P. Vieth (clinical pediatrics), and Samuel Zurik (clinical otolaryngology). Dr. Clifford G. Grulee Jr., assistant professor of pediatrics, has been named director of the division of graduate medicine.

Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education and public health. Programs should be received at least three weeks before the date of meeting.

MARYLAND

Hospital News.—Dr. Russell A. Nelson has been appointed director of the Johns Hopkins Hospital, Baltimore, to succeed Dr. Edwin L. Crosby, director of the hospital since 1946, who has resigned to become executive head of the Joint Commission for the Accreditation of Hospitals. Dr. Nelson since 1947 has been assistant to Lowell J. Reed, Ph.D., vice-president of the Johns Hopkins University and Hospital.

Narcotic Violation.—Dr. John C. Stewart of Baltimore pleaded not guilty in the state court at Baltimore to a violation of the Uniform Narcotic Drug Act of Maryland and on April 18 was found guilty and sentenced to serve three years. His sentence was suspended, and he was placed on probation, the provisions of which were that he should surrender his narcotic registration. He was also fined $1,000.

MASSACHUSETTS

Society News.—At the annual business meeting of the Massachusetts Heart Association, Dr. Lewis M. Hurxthal of Newton was elected president and Dr. James C. McAdams of Fall River, vice-president. Dr. Benedict F. Massell of Brookline and Mr. Charles E. Cotting of Boston were reelected secretary and treasurer, respectively.

Dr. Hertig Appointed Shattuck Professor.—Dr. Arthur T. Hertig of Boston has been appointed Shattuck Professor of Pathological Anatomy at Harvard Medical School, Boston, to succeed Dr. S. Burt Wolbach, who held that office from 1922 until his retirement in 1947. In 1949 Dr. Hertig and Dr. John Rock, Brookline, won the award of the American Gynecological Society for their study of the development of the early human ovum. Dr. Hertig has been teaching and conducting research in pathology at Harvard Medical School and its associated hospitals since 1932, except for two years (1934-1936) when, as a national research fellow at the Carnegie Institution of Washington, D. C., he was engaged in studying the pathology of embryos. He has been professor of pathology at the Boston Lying-In Hospital and the Free Hospital for Women, Brookline, since 1948 and also has served as consultant to the U. S. Naval Hospital at Chelsea and to the Armed Forces Institute of Pathology.

MISSOURI

Dr. Oscar V. Batson Honored.—The University of Missouri, Columbia, recently conferred the honorary degree of doctor of science on Dr. Oscar V. Batson, professor of anatomy and chairman of the department in the Medico-Chirurgical College, Graduate School of Medicine, University of Pennsylvania, Philadelphia, since 1928, and also assistant professor of otolaryngology at the University of Pennsylvania School of Medicine. Dr. Batson served as instructor in pathology at the University of Missouri School of Medicine, St. Louis, and as instructor in anatomy at the University of Wisconsin, Madison. He later became professor of anatomy at the University of Cincinnati and also at the Ohio College of Dental Surgery before accepting appointment in the Pennsylvania Graduate School of Medicine. He was awarded the Wilhelm Conrad Medal by the American Roentgen Ray Society in 1941 and the bronze medal by the American Medical Association in 1942.

NEW YORK

Society News.—Dr. Carlton E. Wertz, Buffalo, has been appointed chairman of the convention committee for the 1953 annual meeting of the Medical Society of the State of New York to be held next May at Hotel Statler, Buffalo, and Dr. William J. Orr, also of Buffalo, has been designated chairman of the local committee on arrangements.

Gift of Rare Book.—The Lancet Society, an organization of physician-specialists, has presented to the State University of New York College of Medicine at Syracuse a rare book containing the anatomical illustrations of Andreas Vesalius. This volume, given in memory of the late Dr. Henry H. Haft, one of the founders of the society, and clinical professor of medicine at the college of medicine, is one of a number of copies, published jointly by the New York Academy of Medicine and the Library of the University of Munich in Germany, with reproductions from the original wood blocks. These blocks were later destroyed in the bombing of Munich during World War II.

New York City

Hartford Memorial Chapel.—The Pauline A. Hartford Memorial Chapel, a new interdenominational chapel for the use of patients, their relatives, and the hospital staff, was recently dedicated at Columbia-Presbyterian Medical Center. The chapel, a gift of the late John A. Hartford, former board chairman of the Great Atlantic and Pacific Tea Company, is named in honor of his wife, who was a patient at Presbyterian Hospital shortly before her death in 1948.

Alumni Elections.—The Alumni Association of the New York University College of Medicine has elected as president Dr. Anthony S. Bogatko, assistant professor of clinical surgery of the College of Medicine. Dr. Harold Brandaleone, assistant clinical professor of medicine at the college and medical director of the Third Avenue Transit System, was named vice-president.——Dr. James W. Smith, clinical professor of ophthalmology, New York University Post Graduate Medical School, was recently elected vice-president of the Alumni Federation of New York University.

NORTH CAROLINA

Man of the Year.—Dr. Thomas Craven of Huntersville was named "Man of the Year" at a dinner of the Huntersville Lions Club. A scroll was presented by Dr. Edward R. Hipp of Charlotte, president of the Mecklenburg County Medical Society, of which Dr. Craven has been a member for more than 30 years. Dr. Craven has served several terms as mayor of Huntersville and is a member of the Mecklenburg Board of Health, the board of the Mecklenburg Tuberculosis Sanatorium, and the Huntersville School Board.

Postgraduate Program.—The 1952-1953 program of year-round postgraduate medical education at James Walker Memorial Hospital in Wilmington began July 1, with Dr. George T. Harrell, professor of internal medicine and director of the department, Bowman Gray School of Medicine of Wake Forest College, Winston-Salem, as visiting chief. Licensed physicians and medical students are invited to attend the daily conferences held from 5 to 6 p. m., and the clinical pathological conference held each Wednesday at 7:30 p. m. No registration fee is required, but all physicians residing outside New Hanover County are requested to register at the information desk in the lobby of the James Memorial Hospital. During the remainder of 1952, the following visiting chiefs will participate in the program: Aug. 19-22, Dr. Robert L. Sanders, Memphis; Sept. 9-12, Dr. Robert B. Lawson, Winston-Salem; Oct. 7-10, Dr. Richard W. TeLinde, Baltimore; Nov. 4-7, Dr. Charles C. Lund, Boston; Dec. 2-5, Dr. Bradley L. Coley, New York.

OHIO

Doctor's Orchestra.—The Doctor's Orchestra of Akron, under the directorship of Dr. Alexander S. McCormick, in June ended its 26th season with its 159th concert. The next season will open with rehearsals in October.

Centennial of Death of Daniel Drake.—Cincinnati recently observed the centennial of the death of Dr. Daniel Drake, the first physician in Cincinnati to receive a diploma (1805). Dr. Drake founded what is now known as the Cincinnati General Hospital and the University of Cincinnati College of Medicine, serving as its first professor of medicine. He was a pioneer in medical journalism west of the Allegheny mountains, notable among his contributions being the treatise on "The Principal Diseases of the Interior Valleys of North America."

Dr. Marion A. Blankenhorn, professor and chairman, department of internal medicine, University of Cincinnati College of Medicine, was the principal speaker at the Drake tombstone in Spring Grove Cemetery, where a bronze plaque was dedicated, replacing the worn inscription. At a banquet at the Vernon

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Manor Hotel, Dr. Frank H. Mayfield, immediate past president, presented to Dr. Cecil Striker, president of the Academy of Medicine, the Daniel Drake gavel, made from the doorsill of Drake's home on Third Street.

A resolution, previously adopted, provides that the new hospital building at the Hamilton County Home is named the Daniel Drake Memorial Hospital. Honorary degrees, conferred by President Raymond Walters of the University of Cincinnati on distinguished guests Dr. Ralph Major of Kansas City, Kan., and Dr. Emmet F. Horine of Brooks, Ky., were previously reported in THE JOURNAL. The *Cincinnati Journal of Medicine* entitled its June, 1952, issue the "Daniel Drake Memorial Edition."

PENNSYLVANIA

Physicians Needed.—The Philadelphia Quartermaster Depot, 2800 South 20th Street, Philadelphia, is in need of a full-time (40 hour week) civilian physician. The annual salary is $5,060. For information telephone Mr. Arthur J. Jones, HO 5-2000. A physician is also needed for a summer camp at Pocono Highland, July 27 to Aug. 27. For information telephone Mr. Weinberg, RI 6-0748.

Society News.—The following medical schools of Pennsylvania have made favorable reply to a resolution approved by the House of Delegates of the Medical Society of the State of Pennsylvania recommending the establishment of departments of physical medicine and rehabilitation at the undergraduate and graduate level: the University of Pennsylvania School of Medicine, Temple University School of Medicine, Woman's Medical College of Pennsylvania, Jefferson Medical College, and Hahnemann Medical College, all of Philadelphia, and the University of Pittsburgh School of Medicine.

Philadelphia

Isotope Laboratory.—The Goldman Isotope Laboratory of the Hahnemann Medical College and Hospital of Philadelphia was officially dedicated June 4 at a banquet in honor of Mr. William Goldman, a trustee of the college, who made possible the establishment of the laboratory. Ralph T. Overman, Ph.D., chief of the training section of the Oak Ridge Institute for Nuclear Studies, was the principal speaker.

Pittsburgh

Society Election.—At the meeting of the Pittsburgh Roentgen Society held June 11, the following officers were elected: Dr. William T. Rice, president; Dr. Joseph E. Malia, vice-president; Dr. Donald H. Rice, secretary; Dr. Newton Hornick, treasurer; and Dr. Samuel G. Henderson, counsellor to the American College of Radiology.

SOUTH DAKOTA

Indian Agency Agreement.—The Bureau of Indian Affairs and the South Dakota State Medical Association have entered into an agreement for use of the fee schedule approved by the association, under which medical services of private physicians will be provided. This agreement is for patients referred to private physicians by the superintendent of the reservation involved and for emergency treatment of eligible Indians who may need care away from the reservation. Authorizations issued by the superintendent of the unit involved must accompany each patient referred to private physicians.

WASHINGTON

Haverhill Fever.—Haverhill fever (epidemic arthritic erythema) has been reported in Clark County, Washington. Two cases have been proved by agglutination in high dilution. Discovery of these cases has been credited to Dr. Edward C. Heyde of Vancouver.

Society News.—At the meeting of the Washington State Obstetrical Association, May 3, in Vancouver, B. C., Dr. Clarence W. Knudson of Seattle was elected president; Dr. Kenneth E. Norris of Yakima, vice-president; and Dr. Lincoln B. Donaldson of Seattle, secretary-treasurer.

WEST VIRGINIA

Joint Health and Welfare Meeting.—The West Virginia Welfare Conference, Inc., and the West Virginia Public Health Association will hold a joint meeting at Jackson's Mill, Aug. 22. Dr. Fred J. Holter, Ph.D., graduate advisor in the school of physical education at West Virginia University, will discuss "Community Health Councils." Mr. H. William Millington of Charleston, executive secretary of the Kanawha Welfare Council, will speak on welfare councils; and Mr. Charles Lively, executive secretary, West Virginia State Medical Association, will present a résumé of the association's fifth annual rural health conference held in June. The joint meeting of the 28 member board of the Welfare Conference and the 16 member council of the PHA, the first in the history of the two organizations, has been arranged to correlate the related programs of the two groups.

GENERAL

Society Election.—At the annual meeting of the American Laryngological Association in Toronto, Canada, May 23-24, Dr. Louis H. Clerf, Philadelphia, was elected president; Dr. J. Mackenzie Brown, Los Angeles, first vice-president; Dr. Edwin N. Broyles, Baltimore, second vice-president; Dr. Harry P. Schenck, New York, secretary; and Dr. Gordon F. Harkness, Davenport, Ia., treasurer.

Summer Course in Gerontology.—The New York University summer school at Chautauqua, N. Y., offers a workshop on problems of gerontology and adult education. The course will be given from July 28 to Aug. 8 under the co-direction of Prof. John Carr Duff of the N. Y. U. School of Education and Wilma T. Donahue, Ph.D., director of the division of gerontology at the University of Michigan Human Adjustment Center. Dr. Karl A. Menninger, Topeka, Kan., Harry A. Overstreet, professor emeritus of philosophy, College of the City of New York, and Mrs. Bonaro Overstreet are among the scheduled lecturers.

Outbreaks of Gastroenteritis.—According to the U. S. Public Health Service, an outbreak of food poisoning was reported by the California Department of Public Health. In a fruit pickers' camp about 75 persons became ill after eating sandwiches prepared from ground bologna and boiled eggs. Laboratory examination revealed Staphylococcus albus and alpha hemolytic Streptococcus. The Massachusetts Department of Health reports an outbreak of gastroenteritis in which 84 of 125 persons became ill after a high school banquet. Examination revealed Salmonella typhimurum in nine cases. Another outbreak occurred two weeks later after a banquet served by the same caterer in another high school.

Traffic Accidents in May.—According to the National Safety Council, more Americans were killed by automobiles this May than in any other May on record. The death toll of 3,160 was 12% over May in 1951. The previous high for May was 3,066 deaths in 1937. The May toll boosted the average increase for the first five months of this year to 4% more than for the comparable period last year. Of 42 states reporting for May, 30 had more deaths than in May a year ago, and 12 had fewer.

In contrast with the sharp increase in deaths reported by the states, 441 reporting cities had 5% fewer deaths than in May of last year. Of the 441 cities, 308 reported no traffic deaths in May. The three largest were Providence, R. I. (248,700); Hartford, Conn. (177,400), and New Haven, Conn. (164,400). For five months 156 still had perfect records. The three largest were: Little Rock, Ark. (102,200); Davenport, Ia. (74,500), and Evanston, Ill. (73,600).

Research at Brookhaven National Laboratory.—One hundred and fifty-four visiting scientists and students will participate in the research program at Brookhaven National Laboratory, Upton, L. I., N. Y., this summer, according to Robert A. Patterson, Ph.D., assistant director of the laboratory. This is nearly as many as the total for the 1950 and 1951 summer programs. The summer program will place Brookhaven's special research facilities in the field of atomic energy at the disposal of scientists and students. Of the 1952 group, 63 are scientists who will participate in research projects related to work they conduct at 35 different universities, colleges, or industrial organizations

which they represent. Ninety-one are either graduate students or undergraduates from 38 different universities and colleges, who will spend the summer as research assistants in study of atomic energy. Many of the scientists will work in the biology or reactor departments. Brookhaven is the northeastern center for nuclear research and development operated under contract with the AEC by Associated Universities, Inc., a nonprofit educational corporation sponsored by nine leading eastern universities.

Prevalence of Poliomyelitis.—According to the National Office of Vital Statistics, the following number of reported cases of poliomyelitis occurred in the United States, its territories and possessions in the weeks ended as indicated:

Area	July 5, 1952	June 28, 1952	July 7, 1951
New England States			
Maine	2	3	..
New Hampshire	..	..	..
Vermont	1	1	1
Massachusetts	2	1	5
Rhode Island	..	..	..
Connecticut	2	2	5
Middle Atlantic States			
New York	24	21	17
New Jersey	2	3	5
Pennsylvania	4	4	7
East North Central States			
Ohio	45	22	7
Indiana	2	9	3
Illinois	4	8	16
Michigan	13	13	21
Wisconsin	3	10	12
West North Central States			
Minnesota	4	2	4
Iowa	27	20	..
Missouri	10	5	6
North Dakota	1	1	1
South Dakota	2	..	1
Nebraska	16	2	7
Kansas	17	19	5
South Atlantic States			
Delaware	..	..	1
Maryland	..	..	1
District of Columbia	..	1	3
Virginia	10	..	4
West Virginia	3	6	1
North Carolina	8	9	6
South Carolina	..	1	3
Georgia	11	16	14
Florida	10	10	10
East South Central States			
Kentucky	2	4	..
Tennessee	12	9	4
Alabama	17	8	22
Mississippi	26	26	16
West South Central States			
Arkansas	10	9	15
Louisiana	19	26	39
Oklahoma	26	22	21
Texas	186	206	58
Mountain States			
Montana	1	5	..
Idaho	1	..	..
Wyoming	..	2	1
Colorado	6	5	21
New Mexico	16	6	2
Arizona	7	2	7
Utah	1	..	2
Nevada	..	..	..
Pacific States			
Washington	14	14	2
Oregon	9	2	2
California	43	39	39
Territories and Possessions			
Alaska	..	..	..
Hawaii	18	6	..
Puerto Rico	..	..	..
Total	639	590	408

Meeting of Persons Subjected to Laryngectomy.—An Institute on Voice Pathology and the first International Meeting of Laryngectomized Persons are announced by the Cleveland Hearing and Speech Center, an affiliate of Western Reserve University. The meeting will be held Aug. 1 and 2 at Harkness Chapel, Bellflower and Ford Drive, on the campus of the university in Cleveland. It is sponsored by the American Cancer Society (Cuyahoga Unit), Cleveland Academy of Medicine, National Cancer Institute of the Institutes of Public Health, Cleveland Otolaryngological Club, the Lost Chord Club of Cleveland, Office of Vocational Rehabilitation of the Federal Security Agency, and the School of Medicine and Speech Department of Western Reserve University.

On Friday, meetings will be held by the sections on laryngeal disease and voice therapy, research on voice, and dysphonias. Saturday morning the sections on surgery in laryngectomy and on rehabilitation of laryngectomized persons will meet. The latter section will present a panel discussion on "Methods of Teaching Esophageal Speech." On Saturday afternoon the first International Meeting of Laryngectomized Persons will be held. Guest speaker at this meeting will be Dr. Charles S. Cameron of New York, president of the American Cancer Society.

The Cleveland Hearing and Speech Center announces that in 1951, 1,992 children and adults received direct therapy and 19,370 persons received indirect service in recreational rehabilitation, public education and training activities. Since 1945, when the center was formed as the result of a merger of the Cleveland Hearing Center and Western Reserve University Speech Clinic, more than 150 laryngectomized persons have been trained in esophageal speech and have participated in the center's Lost Chord Club.

College of Surgeons Meets in New York.—The annual clinical congress of the American College of Surgeons will be held at the Waldorf-Astoria, New York, Sept. 22-26 under the presidency of Dr. Alton Ochsner, New Orleans. On Tuesday a symposium on trauma will be held from 2 to 5 p. m., and at 8:30 p. m. there will be a motion picture symposium on surgery of the heart. On Wednesday a symposium on cancer will be held at 2 p. m. Five panel discussions in gynecology and obstetrics will be held Wednesday, Thursday, and Friday afternoons; problems of neurologic, thoracic, orthopedic, and plastic surgery, and urology will be considered in two panel discussions each on Friday afternoon; and sessions on ophthalmology and otolaryngology will be held Tuesday, Wednesday, and Thursday.

There will be 12 sessions of the forum on fundamental surgical problems, with about 155 papers. Attendance at seven postgraduate courses, to be given from 9 a. m. until noon Tuesday through Friday, is limited to persons registered for them. There will be courses in gynecology and obstetrics, management of fractures, nonmalignant diseases of the gastrointestinal tract, pre and postoperative care of the surgical patient, surgical aspects of pulmonary disease, trauma of the skull and spine, and cardiovascular surgery. The presidential dinner Monday will be followed by an assembly and the presidential meeting. Dr. Donald C. Balfour of Rochester, Minn., will give the 7th Martin Memorial Lecture on "The Evolution of Gastric Surgery." On Wednesday Dr. Sumner L. Koch, Chicago, will give the annual trauma oration and on Friday evening Sir Cecil Wakely of London, England, president of the Royal College of Surgeons, will give the fellowship address at the convocation. A cruise to the Island of Bermuda following the congress has been arranged. Participants will leave New York on Sept. 27 aboard the Queen of Bermuda, returning to New York Oct. 3. Information regarding rates may be obtained from Mr. Leon V. Arnold, 36 Washington Square West, New York 11.

EXAMINATIONS AND LICENSURE

NATIONAL BOARD OF MEDICAL EXAMINERS

NATIONAL BOARD OF MEDICAL EXAMINERS: *Part I*, Sept. 8-10. All centers where there are five or more candidates. Exec. Sec., Dr. John P. Hubbard, 225 S. 15th St., Philadelphia 2.

EXAMINING BOARDS IN SPECIALTIES

AMERICAN BOARD OF ANESTHESIOLOGY: *Oral*. Swampscott, Mass., Sept. 28-Oct. 1. Sec., Dr. C. B. Hickcox, 80 Seymour St., Hartford 15.

AMERICAN BOARD OF DERMATOLOGY AND SYPHILOLOGY: *Written*. Various Centers, September 1953. Final date for filing applications was May 1. All candidates are now required to take the written examination. *Oral*. Philadelphia, October 1953. Ex. Sec., Miss Janet Newkirk, 66 East 66th St., New York 21.

AMERICAN BOARD OF INTERNAL MEDICINE: *Written*. Various centers and overseas, Oct. 20. Closing date for the acceptance of applications for the written examination was May 1. *Oral*. San Francisco, Sept. 3-6; Philadelphia, Nov. 13-14 and Washington, D. C., Nov. 17-18. Exec. Sec.-Treas., Dr. William A. Werrell, 1 West Main Street, Madison 3.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY: *Written*. Various Centers, Feb. 6, 1953. Final date for filing applications is Nov. 1. Sec., Dr. R. L. Faulkner, 2105 Adelbert Road, Cleveland 6.

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AMERICAN BOARD OF OPHTHALMOLOGY: *Written.* Various Centers, January 1953. Final date for filing applications was July 1. *Practical.* Chicago, Oct. 6-10 and New York City, June 6-10, 1953. Sec., Dr. Edwin B. Dunphy, 56 Ivie Road, Cape Cottage, Maine.

AMERICAN BOARD OF ORTHOPAEDIC SURGERY: The deadline for the receipt of applications for the 1953 Part II examinations is Aug. 15. Sec., Dr. Harold A. Sofield, 122 S. Michigan Ave., Chicago.

AMERICAN BOARD OF OTOLARYNGOLOGY: *Written.* Chicago, Oct. 6-10. *Oral.* Chicago, Oct. 6-10 and April 21-25, 1953. Sec., Dr. Dean M. Lierle, University Hospital, Iowa City.

AMERICAN BOARD OF PATHOLOGY: *Written and Oral.* Pathologic Anatomy and Clinical Pathology examination. Chicago, Oct. 9-11. Sec., Dr. William B. Wartman, 303 E. Chicago Ave., Chicago 11.

AMERICAN BOARD OF PEDIATRICS: *Oral.* Chicago, Oct. 24-26; Boston, Dec. 5-7. Exec. Sec., Dr. John McK. Mitchell, 6 Cushman Road, Rosemont, Pa.

AMERICAN BOARD OF PREVENTIVE MEDICINE AND PUBLIC HEALTH: Cleveland, Oct. 18-20. Sec., Dr. E. L. Stebbins, 615 N. Wolfe St., Baltimore.

AMERICAN BOARD OF PROCTOLOGY: *Oral and Written.* Philadelphia, Sept. 27-28. Sec., Dr. Louis A. Buie, 102-110 Second Ave., S.W., Rochester, Minn.

AMERICAN BOARD OF PSYCHIATRY AND NEUROLOGY: New York City, Dec. 15-16. Final date for filing applications is Sept. 15. Sec.-Treas., Dr. David A. Boyd, Jr., 102-110 Second Ave. S.W., Rochester, Minn.

AMERICAN BOARD OF RADIOLOGY: *Oral.* Dec. 1-7. Final date for filing application was June 1. Sec., Dr. B. R. Kirklin, 102-110 Second Ave., S.W., Rochester, Minn.

AMERICAN BOARD OF SURGERY: *Written.* Various Centers. October 1952. Final date for filing application was July 1. *Written.* Various Centers, March 1953. Final date for filing application is Dec. 1. Sec., Dr. J. Stewart Rodman, 225 S. 15th St., Philadelphia.

AMERICAN BOARD OF UROLOGY: *Written.* Various Centers, December. *Oral.* Chicago, Feb. 7-11. Sec., Dr. Harry Culver, 30 Westwood Road, Minneapolis 16, Minn.

BOARD OF THORACIC SURGERY: *Written.* Various Centers, Sept. 5. Sec., Dr. William M. Tuttle, 1151 Taylor Ave, Detroit 2.

MEETINGS

ALASKA TERRITORIAL MEDICAL ASSOCIATION, Anchorage, Aug. 21-23. Dr. William P. Blanton, P. O. Box 2569, Juneau, Secretary.

AMERICAN ASSOCIATION OF OBSTETRICIANS, GYNECOLOGISTS AND ABDOMINAL SURGEONS, The Homestead, Hot Springs, Va., Sept. 4-6. Dr. William F. Mengert, 2211 Oak Lawn Ave., Dallas, Texas, Secretary.

AMERICAN CONGRESS OF PHYSICAL MEDICINE, Roosevelt Hotel, New York, Aug. 25-29. Dr. Frances Baker, One Tilton Ave., San Mateo, Calif., Secretary.

AMERICAN HOSPITAL ASSOCIATION, Philadelphia, Sept. 15-18. Mr. George Bugbee, 18 East Division St., Chicago 10, Executive Director.

AMERICAN PHYSIOLOGICAL SOCIETY, New Orleans, Sept. 4-6. Dr. E. F. Adolph, University of Rochester School of Medicine and Dentistry, Rochester, N. Y., Secretary.

AMERICAN SOCIETY OF MAXILLOFACIAL SURGEONS, Hotel del Coronado, San Diego, Calif., Sept. 10-13. Dr. Casper M. Epsteen, 25 East Washington St., Chicago 2, Secretary.

BIOLOGICAL PHOTOGRAPHIC ASSOCIATION, Hotel New Yorker, New York, Sept. 10-12. Mr. Lloyd E. Varden, Pavelle Color, Inc., 533 W. 57th St., New York 19, Secretary.

MEDICAL SOCIETY OF DELAWARE, Rehoboth, Sept. 8-10. Dr. Andrew M. Gehret, 822 North American Bldg., Wilmington, Secretary.

MONTANA MEDICAL ASSOCIATION, Florence Hotel, Missoula, Sept. 18-21. Mr. L. R. Hegland, 104 North Broadway, Billings, Executive Secretary.

NATIONAL MEDICAL ASSOCIATION, Chicago, Aug. 11-15. Dr. John T. Givens, 1108 Church St., Norfolk 10, Va., General Secretary.

NEUROSURGICAL SOCIETY OF AMERICA, The Cloister, Sea Island, Ga., Sept. 18-20. Dr. C. D. Hawkes, 22 North Manassas St., Memphis 5, Tenn., Secretary.

NEVADA STATE MEDICAL ASSOCIATION, Reno, Aug. 21-23. Dr. William A. O'Brien III, 505 Chestnut St., Reno, Secretary.

NEW HAMPSHIRE MEDICAL SOCIETY, Mt. Washington Hotel, Bretton Woods, Sept. 7-9. Dr. Deering G. Smith, 44 Chester St., Nashua, Secretary.

NORTH PACIFIC PEDIATRIC SOCIETY, Challenger Inn, Sun Valley, Idaho, Sept. 19-20. Dr. S. Gorham Babson, 1107 S.W. 13th Ave., Portland 5, Ore., Secretary.

NORTH PACIFIC SOCIETY OF INTERNAL MEDICINE, Sun Valley, Idaho, Sept. 19-20. Dr. Robert L. King, 1115 Terry Ave., Seattle 1, Wash., Secretary.

NORTH TEXAS-SOUTHERN OKLAHOMA FALL CLINICAL CONFERENCE, Wichita Falls, Texas, Sept. 17. Dr. E. Aubrey Cox, Hamilton Bldg., Wichita Falls, Texas, Chairman.

RENO SURGICAL SOCIETY CONFERENCE, Reno, Nevada, Aug. 21-23. Dr. Olin C. Moulton, 130 N. Virginia St., Reno, Nevada, Chairman.

ROCKY MOUNTAIN RADIOLOGICAL SOCIETY, Denver, Aug. 7-9. Dr. Maurice D. Frazer, 1037 Stuart Bldg., Lincoln, Neb., Secretary.

U. S. CHAPTER, INTERNATIONAL COLLEGE OF SURGEONS, Conrad Hilton Hotel, Chicago, Sept. 2-5. Dr. Arnold S. Jackson, 1516 Lake Shore Drive, Chicago, Executive Secretary.

UTAH STATE MEDICAL ASSOCIATION, Salt Lake City, Sept. 4-6. Dr. T. C. Weggeland, 42 S. Fifth East St., Salt Lake City, Secretary.

VERMONT STATE MEDICAL SOCIETY, Mt. Washington Hotel, Bretton Woods, N. H., Sept. 7-9. Dr. James P. Hammond, 128 Merchants Row, Rutland, Secretary.

WASHINGTON STATE MEDICAL ASSOCIATION, Olympic Hotel, Seattle, Sept. 13-17. Dr. Bruce Zimmerman, 338 White-Henry-Stuart Bldg., Seattle, Secretary.

INTERNATIONAL

AMERICAN CONGRESS OF INDUSTRIAL MEDICINE, Rio de Janeiro, Brazil, Sept. 20-28. General Secretarial Office: Calle Arenales No. 981 Buenos Aires, Argentina.

AUSTRALASIAN MEDICAL CONGRESS, Melbourne Victoria, Australia, Aug. 22-30. Dr. C. H. Dickson, Medical Society Hall, 426 Albert St., East Melbourne, Victoria, Australia, General Secretary.

EUROPEAN CONGRESS OF CARDIOLOGY, University of London, Bloomsbury, W.C.1, England, Sept. 10-12. Dr. K. Shirley Smith, 35 Wimpole St., London, W.1, England, Secretary.

EUROPEAN SOCIETY OF CARDIOVASCULAR SURGERY, Strasbourg, France, Oct. 3-4. Sir James Learmonth, Department of Surgery, University New Buildings, Edinburgh 8, Scotland.

INTERAMERICAN CARDIOLOGICAL CONGRESS, Buenos Aires, Argentina, Aug. 31-Sept. 7. Dr. Blas Moia, Larrea 1132, Buenos Aires, Argentina, Secretary-General.

INTER-AMERICAN CONGRESS OF PUBLIC HEALTH, Havana, Cuba, Sept. 26-Oct. 1. Pan-American Sanitary Bureau, 2001 Connecticut Ave., Washington, D. C.

INTER-AMERICAN CONGRESS OF RADIOLOGY, Mexico City, Mexico, Nov. 2-8. Dr. Guido Torres Martinez, Marsella No. 11, Mexico, D.F., Secretary-General.

INTERNATIONAL CONGRESS OF ANTHROPOLOGY AND ETHNOLOGY, Vienna, Austria, Sept. 1-8. For information write: Secretaries, Royal Anthropological Institute, 52 Upper Bedford Place, London, W.C.1, England.

INTERNATIONAL CONGRESS ON DISEASES OF THE CHEST, Rio de Janeiro, Brazil, Aug. 24-30. Mr. Murray Kornfeld, 112 East Chestnut St., Chicago 11, Illinois, Executive Secretary.

INTERNATIONAL CONGRESS OF HAEMATOLOGY, Mar del Plata, Argentina, Sept. 21-26. Dr. Carlos Reussi, Anchorena 1710, Buenos Aires, Argentina, Secretary.

INTERNATIONAL CONGRESS OF THE HISTORY OF MEDICINE, Nice-Cannes, France, and Monaco, Sept. 8-14. Dr. F. A. Sondervorst, 124 Avenue des Allies, Louvain, Belgium, Secretary-General.

INTERNATIONAL CONGRESS ON HYDATID DISEASE, Santiago, Chile, Nov. 21-24. Organizing Committee, P. O. Box 9183, Santiago, Chile.

INTERNATIONAL CONGRESS OF INTERNAL MEDICINE, Friends House, London, N.W.1, Eng., Sept. 15-18. Sir Harold Boldero, 12 Pall Mall East, London, S.W.1, England, Secretary.

INTERNATIONAL CONGRESS OF MEDICAL PRESS, Venice, Italy, Oct. 4-5. Dr Bruno de Biasio, S. Marco 4646, Venice, Italy, Secretary.

INTERNATIONAL CONGRESS ON MEDICAL RECORDS, London, England, Sept. 7-12. Miss Gwen Perkins, 120 C Street S.E., Washington, D. C., Chairman.

INTERNATIONAL CONGRESS OF MILITARY MEDICINE AND PHARMACY, Montevideo, Uruguay, March 1-7, 1953. Dirrección General del Servico de Sanitad Militar, 8 de Octubre y Mariano Moreno, Montevideo, Uruguay, Secretariat of the Congress.

INTERNATIONAL CONGRESS ON NEUROPATHOLOGY, Rome, Italy, Sept. 8-13. Dr. Armando Ferraro, 722 W. 168th St., New York, N. Y., U. S. A., Secretary General.

INTERNATIONAL CONGRESS OF OTORHINOLARYNGOLOGY, Amsterdam, Netherlands, June 8-15, 1953. Dr. W. H. Struben, J. J. Viottastraat 1, Amsterdam, Netherlands, Secretary.

INTERNATIONAL CONGRESS OF UROLOGY, The Waldorf-Astoria, New York, N. Y., U. S. A., Sept. 15-18. Dr. John A. Taylor, 2 East 54th St., New York, N. Y., U. S. A., Secretary-General.

INTERNATIONAL HOSPITAL CONGRESS, London, England, May 25-30, 1953. Capt. J. E. Stone, 10 Old Jewry, London, EC2, England, Hon. Secretary.

INTERNATIONAL STUDY CONFERENCE ON CHILD WELFARE, Bombay, India, Dec. 5-12. For information write: All India Save the Children Committee, 5 Carmichael Road, Bombay, India.

INTERNATIONAL UNION AGAINST TUBERCULOSIS, Rio de Janeiro, Brazil, Aug. 24-27. Prof. Etienne Bernard, 66 Blvd. St. Michel, Paris 6e, France, Secretary-General.

MEDICAL WOMEN'S INTERNATIONAL ASSOCIATION, Vichy, France, Sept. 12-16. Dr. Margaret M. Wurts, 27 East Wellesley Road, Montclair, N. J., U. S. A., National Secretary.

NEURORADIOLOGIC SYMPOSIUM, Stockholm, Sweden, Sept. 17-20. Docent Ake Lindbom, Symposium Neuroradiologicum, Serafimerlasarettet, Stockholm K., Sweden, Secretary.

WORLD CONGRESS OF JEWISH PHYSICIANS, Jerusalem, Israel, Aug. 10-14. Secretariat: % Israel Medical Association, Rehov Mesilat Yesharim, Beth Kovatz, Jerusalem, Israel.

WORLD CONGRESS OF MEDICINE, Montecatini, Italy, Oct. 16-18. Secretariat: Corso Trieste, 65, Rome, Italy.

WORLD FEDERATION OF MENTAL HEALTH, Brussels, Belgium, Aug. 25-Sept. 1. Dr. J. R. Rees, 19 Manchester St., London, W.1, England, Secretary.

WORLD MEDICAL ASSOCIATION, Athens, Greece, Oct. 12-16. Dr. Louis H. Bauer, 2 East 103d St., New York 29, N. Y., Secretary General

DEATHS

Ireland, Merritte Weber ✠ major general, U. S. Army, retired, Washington, D. C., formerly, for more than 12 years, Surgeon General of the Army, died in Walter Reed Hospital July 5, aged 85. Born in Columbia City, Ind., the son of a physician, General Ireland received his first degree in medicine from the Detroit College of Medicine in 1890. He received a second degree from Jefferson Medical College in Philadelphia the following year and then was commissioned an assistant surgeon in the Army. He served in Cuba during the Spanish-American War. During the Mexican expedition led by Gen. John J. Pershing he was post surgeon at Fort Sam Houston, Texas and later went to France with General Pershing, where he headed the medical service of the American Expeditionary Force. General Ireland was largely responsible for the development of modern concepts of field medicine during World War I. He served as Surgeon General from Oct. 4, 1918, until his retirement from the Army on May 31, 1931. His term of office saw the creation of the Army Medical Center on the grounds of Walter Reed Army Hospital. Among General Ireland's awards were the Distinguished Service Medal, Commander of the Legion of Honor of France, Companion of the Order of the Bath of Great Britain, and Grand Officer of the Order of Polonia Restituta. In 1945 he was awarded the William Freeman Snow Medal for distinguished service to humanity from the American Social Hygiene Association, and in April, 1945, received a citation for distinguished service to humanity from the Medical Society of the District of Columbia. General Ireland served as a delegate from the U. S. Army to the American Medical Association in 1908, 1909, and 1910, and later was a member of its Council on Medical Education and Hospitals. He was past president of the National Board of Medical Examiners, Association of the Military Surgeons of the United States, and the American College of Surgeons. He was formerly secretary of the Gorgas Memorial Institute of Tropical and Preventive Medicine, a fellow and ex-governor of the American College of Physicians, a fellow of the Royal College of Surgeons of Edinburgh, and a member of the American Psychiatric Association. He had been a director of the Columbia Hospital for Women and Lying-In Asylum, Garfield Memorial Hospital, and the United States Soldiers Home Hospital. He delivered the William Potter Memorial Lecture at Jefferson Medical College in 1939. In 1947 he resigned as president of the Army Mutual Aid Association after 18 years of service and as a director of that organization for 32 years. General Ireland received LL.D. degrees from Jefferson in 1919, Gettysburg (Pa.) College in 1922, and Syracuse (N. Y.) University in 1935 and an A.M degree from the University of Michigan in Ann Arbor in 1920.

LeBel, Louis Jean Baptiste ✠ Nutley, N. J.; born [illegible] N. J., Jan. 26, 1895; University of Virginia Department of Medicine, Charlottesville, 1921; specialist certified by the American Board of Dermatology and Syphilology; founder and a past president of the Northern New Jersey Dermatological Society; member of the American Academy of Dermatology and Syphilology; member of the professional staff, Council on Medical Education and Hospitals, American Medical Association in Chicago; at one time taught at Columbia University College of Physicians and Surgeons in New York; for many years affiliated with St. Mary's Hospital in Passaic, where he was president of the medical staff from 1939 to 1941 and where he died May 20, aged 57, of subacute bacterial endocarditis.

Curtis, Elmer Eaton ✠ medical director, captain, U. S. Navy (retired), Vallejo, Calif.; born in Hiawatha, Kan., Aug. 7, 1877; St. Louis University School of Medicine, 1905; commissioned a lieutenant (jg) in the Medical Corps of the U. S. Navy on July 12, 1907; attained the rank of captain on July 1, 1929, and on Sept. 1, 1941, was placed on the retired list; during World War I served aboard the transports USS Powhatan and USS Mount Vernon, engaged in ferrying troops across the Atlantic; after attending the Naval War College, Newport, R. I., in 1933 was assigned to the staff of the commander, Battle Force, U. S. Fleet, as force medical officer; recalled to active duty at the outbreak of World War II, and assigned as medical officer in command of the Naval Dispensary, Treasure Island, Calif.; in 1942, assumed command of the Naval Hospital, Treasure Island, San Francisco; was released from active duty in 1945 and returned to the retired list; died in the Naval Hospital, Mare Island, May 5, aged 74, of lymphosarcoma of small intestine, peritonitis and bronchopneumonia.

Levy, Joseph ✠ New Rochelle, N. Y.; born in New York April 10, 1901; Johns Hopkins University School of Medicine, Baltimore, 1927; specialist certified by the American Board of Internal Medicine; fellow of the American College of Physicians; member of the Latin American Congress of Physical Medicine, Aero Medical Association, International Society of Internal Medicine, American Academy of Sciences, American Geriatrics Society, Israel Medical Association, Westchester Heart Association, and New Rochelle Hospital Association; member of the Phi Delta Epsilon Fraternity and a founder of Tau Alpha Omega, a fraternity at City College; during World War II a flight surgeon with the rank of major in the Army Medical Corps, serving in Africa and the Philippines; adjunct physician, Montefiore Hospital for Chronic Diseases in New York; attending physician, New Rochelle Hospital; died in San José, Costa Rica, recently, aged 50, of coronary occlusion, after delivering a paper at the fourth annual convention of the Latin American Congress of Physical Medicine.

Jostes, Frederick Augustus ✠ St. Louis; born in St. Louis Aug. 14, 1895; Washington University School of Medicine, St. Louis, 1920; specialist certified by the American Board of Orthopaedic Surgery; member of the American Orthopaedic Association, Clinical Orthopaedic Society, and the American Academy of Orthopaedic Surgeons; fellow of the American College of Surgeons; president of the Missouri Society for Crippled Children and Adults and first vice-president of the Mississippi Valley Medical Society; served during World War II; assistant professor of clinical orthopedic surgery at his alma mater; affiliated with St. Louis County Hospital in Clayton, Bernard Free Skin and Cancer Hospital, Evangelical Deaconess, St. Louis Children's, and Jewish hospitals, and the Barnes Hospital, where he died May 19, aged 56, of lymphosarcoma.

White, Vivian Parley ✠ Salt Lake City; born in Salt Lake City, Sept. 12, 1896; Harvard Medical School, Boston, 1923; specialist certified by the American Board of Otolaryngology; member of the American Academy of Ophthalmology and Otolaryngology and the Pacific Coast Oto-Ophthalmological Society, of which he had been vice-president; immediate past president of Utah State Medical Association; past president of the Utah State Ophthalmological Society; clinical lecturer in surgery (otolaryngology) at the University of Utah College of Medicine, where he had been instructor in anatomy of the head and neck from 1925 to 1927; affiliated with Salt Lake County General Hospital and Dr. W. H. Groves Latter-Day Saints Hospital, where he died May 13, aged 55, of carcinoma of the intestine.

Albanese, Nicholas Anthony ✠ Columbus, Ohio; Starling-Ohio Medical College, Columbus, 1914; served during World Wars I and II; affiliated with St. Ann's Maternity Hospital; died April 26, aged 59, of myocardial infarction.

Bartholomew, Alfred Castle ✠ Fort Wayne, Ind.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1901; served during World War I; died in Methodist Hospital April 27, aged 73, of myocardial infarction.

Bennett, Charles Lenzo ✠ Kalamazoo, Mich.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1904; past president of the Kalamazoo Academy of Medicine; formerly practiced in Gobleville, where he had been on the village council and school board; formerly vice-president and

✠ Indicates Member of the American Medical Association.

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director of the State Bank in Gobles; affiliated with Bronson Hospital and Borgess Hospital, where he died April 22, aged 76, of pneumonia and arteriosclerotic heart disease.

Denison, Edward Lyman, Jensen Beach, Fla.; Northwestern Medical College, St. Joseph, Mo., 1892; Illinois Medical College, Chicago, 1895; formerly practiced in Chicago, where he was affiliated with St. Luke's Hospital; died April 27, aged 82, of coronary occlusion.

Elias, Francis Leander ✦ Wymore, Neb.; University of Kansas School of Medicine, Kansas City, 1910; past president of Gage County Medical Society; affiliated with Lutheran Hospital in Beatrice, where he died March 3, aged 68, of coronary thrombosis.

Flowers, Earl Newton ✦ Clarksburg, W. Va.; Johns Hopkins University School of Medicine, Baltimore, 1919; served as city health officer; veteran of World War I; died April 12, aged 57.

Gaskill, Henry Kennedy ✦ Hendersonville, N. C.; Jefferson Medical College of Philadelphia, 1906; member of the Medical Society of the State of Pennsylvania; formerly practiced in Philadelphia, where he was professor of dermatology at the Woman's Medical College of Pennsylvania; served during World War I; died April 11, aged 79 .

Gulbrandsen, Lyder Oliver ✦ Viroqua, Wis.; Marquette University School of Medicine, Milwaukee, 1927; served during World Wars I and II; died in La Crosse, recently, aged 51, of coronary occlusion.

Hamer, Clemen ✦ Glendale, Calif.; College of Medical Evangelists, Loma Linda and Los Angeles, 1924; affiliated with Behrens Memorial Hospital, Physicians and Surgeons Hospital, and Glendale Sanitarium and Hospital, where he was a member of the board of directors and where he died April 1, aged 68, of pneumonia.

Hemstead, Werner ✦ Minneapolis; Omaha Medical College, 1882; died in Rochester, Minn., March 11, aged 91, of bronchopneumonia and cerebral infarcts.

Henriksen, Henry George, Northfield, Minn.; Bennett College of Eclectic Medicine and Surgery, Chicago, 1897; also a graduate in pharmacy; died March 30, aged 82, of carcinoma of the lungs.

Herzog, Charles E. ✦ Stormville, N. Y.; Long Island College Hospital, Brooklyn, 1922; connected with the Department of Correction; killed April 23, aged 53, when his automobile collided with a truck.

Hirst, Jesse Watson, St. Petersburg, Fla.; Jefferson Medical College of Philadelphia, 1893; for many years a Presbyterian medical missionary in Korea, and at one time court physician to the emperor; died in St. Anthony's Hospital April 28, aged 88, of cerebral vascular accident.

Hively, Howard Dayton ✦ Parkersburg, W. Va.; University of Louisville (Ky.) Medical Department, 1912; formerly medical director of the West Virginia Coal and Coke Corporation in Omar; at one time practiced in Charleston, where he was affiliated with Charleston General Hospital; died April 7, aged 66, of coronary thrombosis and arteriosclerosis.

Hodgson, Thomas Cady ✦ Berlin, Conn.; University of Toronto Faculty of Medicine, Toronto, Canada, 1894; served as health officer and medical examiner; died in Hartford April 21, aged 82, of internal carotid thrombosis.

Hofmann, Erich Manfred ✦ Wooster, Ohio; Thüringische Landesuniversität Medizinische Fakultät, Jena, Thuringia, Germany, 1919; died March 4, aged 63.

Hopper, Henry Paine, Saucier, Miss.; Kentucky School of Medicine, Louisville, 1904; for many years county physician; died in the Veterans Administration Hospital, Biloxi, April 3, aged 78, of pulmonary edema and arteriosclerotic heart disease.

Hutchings, Charles Wyatt ✦ Syracuse, N. Y.; Syracuse University College of Medicine, 1926; member of the American Psychiatric Association; served during World War II; assistant director of the Syracuse State School of the New York State Department of Mental Hygiene, Fairmount; formerly on the staff of the Marcy (N. Y.) State Hospital and assistant director of the Manhattan State Hospital, Wards Island, New York City; died in Syracuse Memorial Hospital April 15, aged 52, following a gastrectomy.

Imbrie, Clarence Elwood ✦ Butler, Pa.; Baltimore Medical College, 1904; affiliated with Butler County Memorial Hospital; died April 13, aged 77, of coronary occlusion.

MacDonald, Aeneas E. ✦ Minneapolis; Queen's University Faculty of Medicine, Kingston, Canada, 1901; affiliated with St. Mary's and Asbury hospitals; died April 11, aged 76, of cerebral hemorrhage and arteriosclerosis.

McGarvah, Joseph Andrew ✦ Detroit; Detroit College of Medicine, 1905; affiliated with Woman's Hospital; died March 20, aged 69, of carcinoma of the bile ducts.

Madison, William Davis ✦ Peoria, Ill.; Drake University College of Medicine, Des Moines, 1912; affiliated with Florence Crittenton Home and Methodist Hospital, where he died April 28, aged 69, of coronary thrombosis.

Marcussen, Robert Monroe ✦ Menlo Park, Calif.; Cornell University Medical College, New York, 1943; city councilman; served during World War II; Commonwealth Fund Fellow in Medicine at his alma mater, 1947-1948; in 1949-1950 Fellow in Neuropsychiatry at Stanford University School of Medicine in San Francisco, where he had been clinical instructor in medicine; died April 13, aged 33.

Martin, Solomon Claiborne Jr., West Palm Peach, Fla.; Barnes Medical College, St. Louis, 1893; died recently, aged 81, of myocardial disease and congestive heart failure.

Massoud, Mittry Abi ✦ Pineora, Ga.; Maryland Medical College, Baltimore, 1904; died April 30, aged 76, of coronary heart disease.

Maxson, John Child, Campbell, Calif.; University Medical College of Kansas City, Mo., 1893; served during World War I; died in San Jose March 29, aged 85, of mesenteric thrombosis.

Merrill, Adelbert Samuel ✦ Manchester, N. H.; Tufts College Medical School, Boston, 1908; specialist certified by the American Board of Radiology; member of the American Roentgen Ray Society, New England Roentgen Ray Society and the American College of Radiology; affiliated with Elliott Hospital; died in Concord April 7, aged 76.

Mitchell, Robert Lee ✦ Vinita, Okla.; University of Arkansas School of Medicine, Little Rock, 1904; served overseas during World War I; affiliated with Eastern State Hospital; at one time on the staff of Veterans Administration Hospital in Houston, Texas; for many years affiliated with Veterans Administration Hospital in Muskogee, where he died May 15, aged 76, of coronary thrombosis.

Moncure, Turner Ashby, Baltimore; Medical College of Virginia, [redacted]d, 1912; clinic chief of the Presbyterian Eye, Ear and [redacted]harity Hospital; died in the Lutheran Hospital April [redacted]5, of arteriosclerotic cardiovascular disease.

[redacted]ons, James Franklin, Greenville, Miss.; Mississippi Medical College, Meridian, 1907; on the staff of the Kings Daughters Hospital; died March 27, aged 68, of cerebral hemorrhage.

Smith, John McNeill ✦ Rowland, N. C.; Jefferson Medical College of Philadelphia, 1908; died recently, aged 67, of cerebral hemorrhage and arteriosclerosis.

Townsend, Mary Ella, Atlantic City, N. J.; Woman's Medical College of Pennsylvania, Philadelphia, 1895; died in Camden March 11, aged 83, following an operation for cancer.

White, Thomas Francis ✦ Baltimore; University of Maryland School of Medicine, and College of Physicians and Surgeons, Baltimore, 1920; served as health officer-at-large for Baltimore City; died March 6, aged 61, of coronary thrombosis.

Willson, Pleas, Newborn, Ga.; Atlanta College of Physicians and Surgeons, 1901; died March 14, aged 71, of cerebral hemorrhage and hypertension.

Young, Louise Sanford, El Paso, Texas; Illinois Medical College, Chicago, 1905; University of Louisville (Ky.) Medical Department, 1905; died April 20, aged 83, of arteriosclerosis.

GOVERNMENT SERVICES

NAVY

Construction Projects to Provide 2,300 Hospital Beds.—Plans to build a new permanent hospital at Norfolk, Va., and major permanent additions to existing hospitals at Great Lakes, Ill., and San Diego, Calif., have been announced by the Navy. The construction, which will begin next year, will provide a total of 2,300 additional beds. The largest of the projects will be a 1,000 bed addition to the naval hospital at San Diego. The addition will be a multistory structure and will include operating rooms, x-ray facilities, and messing areas.

The new hospital to augment medical facilities in the Norfolk area will contain 800 beds initially, with provision for expansion to 1,500 beds. The 500-bed addition to the naval hospital at the Great Lakes Naval Training Center will be a multistory permanent structure. The original hospital was built in 1911.

Study of Protein Metabolism.—Henry Borseck, professor of biochemistry at the California Institute of Technology, addressed the Naval School of Aviation Medicine at Pensacola on July 7 on "Newer Aspects of Protein Metabolism." Dr. Borseck was on his way to Paris, where he will lecture on that subject. While in Pensacola he completed initial planning with Captain Ashton Graybiel (MC), Director of Research, and Capt. James L. Rolland (MC), Commanding Officer, preparatory to setting up a cooperative study on protein metabolism sponsored by the California Institute of Technology and the U. S. Naval School of Aviation Medicine.

Personal.—Capt. C. W. Shilling (MC) director, research division, Bureau of Medicine and Surgery, was guest speaker at the annual open house of the Worcester Foundation for Experimental Biology June 14. Captain Shilling spoke on "The Usefulness of Useless Research." Captain Shilling also attended the dedication of the Aviation Medical Acceleration Laboratory at Johnsville, Pa., June 17.

AIR FORCE

Study of Human Adaptation to High Altitudes.—Brig. Gen. Otis O. Benson Jr., commandant of the Air Force School of Aviation Medicine, and a party of military and civilian scientists, have flown to a remote laboratory in Peru, where human adaptation to high altitudes is being investigated. The Institute of Andean Biology, an outpost of the University of San Marcos in Lima, is perched on the upper slopes of the Andes at the mining town of Morococha, one of the loftiest inhabited spots on earth. The town is 90 miles from Peru's sea-coast capital on a plateau 14,900 feet up.

Dr. Alberto Hurtado, the Peruvian physician who runs the Institute, is a Harvard graduate and former research worker at the Mayo Foundation. He has chosen the Indian descendants of the Incas who live on the towering heights of his native land for his special field of study.

The Indians at Morococha toil in the mines at altitudes up to 18,000 ft., where an Air Force flyer is required to wear an oxygen mask, and for relaxation play football in the hard-driving English style. The changes in their physiological processes after centuries of existence on those dizzy heights are of vital interest to the Air Force.

Dr. Hurtado holds a contract with the Air Force to learn what these changes are, and to search for possible ways in which they might be speeded up. It is to settle the final terms of this contract that General Benson's group is flying to Peru. The School of Aviation Medicine is the Air Force research organization which administers the high-altitude project. With the General are other specialists, among them Col. Paul A. Campbell, director of research at the aeromedical school. From the University of California at Berkeley, Dr. John H. Lawrence, director of the Donner Laboratory of Medical Physics, and William Siri, a research physicist, flew to Randolph Field to join the party. Also in the group is Dr. Peter Hoessly, assistant professor of medicine at the University of Utah.

VETERANS ADMINISTRATION

Increased Pay for Disabled Veterans.—Almost 120,000 blind, crippled and tuberculous veterans of all wars and peacetime service will receive increased payments in their compensation checks due Sept. 1, 1952, under Public Law 427 signed by the President June 30. Veterans who are not on the compensation rolls and are covered by the new law should apply at their nearest VA Regional Office.

Veterans who will receive the increased checks are those who have been awarded statutory allowances for the loss, or loss of use, of either or both hands or feet, for blindness, and for total deafness (in combination with total blindness). Veterans who are receiving a minimum monthly rate of compensation for arrested tuberculosis will also receive increased checks. Statutory allowances are paid in addition to the basic compensation rates, which are based on the degree of disability and range from $15.75 to $172.50.

The new law authorizes for the first time for World War II veterans and veterans with service since the beginning of the Korean conflict a minimum monthly rate for arrested tuberculosis and a statutory allowance for the loss, or loss of use, of a creative organ. Up to now these benefits have been available under existing law to certain World War I veterans only. Following are the increases for veterans disabled in wartime or since the Korean conflict started:

1. Monthly statutory allowance for the anatomical loss, or loss of use, of one hand or one foot, or blindness of one eye (having only light perception) increased from $42 to $47. This is payable in addition to monthly rate of compensation.

2. Monthly rate of compensation for the anatomical loss, or loss of use, of both hands, both feet, blindness, total deafness (in combination with total blindness), and various combinations of such disabilities increased from a range of $240 to $360, to a range of $266 to $400. Additional amounts are payable for a wife, children, or dependent parents in these cases and in all other service-connected cases in which the veteran's disability is rated 50% or more. The monthly rates of such additional compensation in totally disabled cases range from $21 to $91, depending on the number and type of dependents. The new law does not increase these additional amounts.

3. The minimum monthly rate of compensation for service-incurred tuberculosis that has been arrested is increased from $60 to $67 and extended to cover World War II veterans and veterans with service since the start of the Korean conflict.

4. Monthly statutory allowance for loss, or loss of use, of creative organ is increased from $30 to $47 and extended to cover World War II veterans and veterans with service since the start of the Korean conflict.

5. Certain seriously disabled World War I veterans, with service-connected disabilities, will receive increased monthly payments—from $198 to $220 for totally blind veterans; from $258 to $286 for totally blind veterans who have lost one or more limbs; and from $60 to $67 for veterans who need the regular aid and attendance of another person.

These new wartime rates also are payable for peacetime service if the specific disabilities were incurred in line of duty as the direct result of armed conflict or while engaged in extra hazardous service, including service under conditions simulating war. Rates of compensation for disabilities incurred during other peacetime service are 80% of wartime rates.

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FOREIGN LETTERS

BRAZIL

International Congress of Surgery.—The International Congress of Surgery was held at Madrid, from May 19 to 25, and was attended by more than 2,000 surgeons of many different specialties, coming from 37 countries. Some 500 papers were presented, and films were shown to demonstrate various surgical techniques. For the first time in Europe, with the cooperation of Remington Rand Inc., color television was produced by the "vericolor" process, and these operations were transmitted on television from the "Cidade Universitaria" (University Town). At the closing ceremony, paying special homage to the memory of the great Spanish scientist Ramon y Cajal, the following speakers were heard: the minister of education, the dean of the university, Prof. Gregorio Marañon, and the secretary of the International Congress, Prof. Alfonso de la Fuente. During this ceremony the head of the Brazilian delegation, Prof. Rodolfo de Freitas, acknowledged the privilege of São Paulo being the place chosen for the 9th International Congress of Surgery and invited surgeons from all over the world to visit Brazil in 1954. At the meeting of the house of delegates it was decided that a building be constructed in São Paulo as a center for meetings of the members of the "Capítulo Brasileiro" (Brazilian chapter) and of the South American zone of the International College of Surgeons. Dr. Rudolph Nissen was elected president of the next congress, and among the future vice-presidents are the Brazilian surgeon Prof. Carlos Gama and Prof. Manuel Manzanolla from Mexico.

Ovarian Pregnancy.—A study on ovarian pregnancy was published by Drs. Domingos Delascio and Luidoso Credidio. They presented a complete historical review commencing with the De Sanctis Maurice case, which is considered to be the first recorded, in the year 1682. They recalled the work of Willigh, who insisted on the necessity for microscopic investigation for a diagnosis of the disease and the criticism of Lawson Tait about cases erroneously diagnosed. The English master referred to a case of a dermoidal tumor described as an ovarian pregnancy. The formulation of the four fundamental conditions for safe diagnosis of this ectopic implantation by Otto Spiegelberg in 1878 is mentioned. Drs. Delascio and Credidio record the study of Catherine van Tussembroeck, in the year 1899, in which, based on microscopic investigations, she was able to establish the diagnosis of ovarian pregnancy. The cause of ovarian pregnancy has been the object of much controversy. The authors believe that ovarian pregnancy may be caused by disturbance of two mechanisms: namely those of ovulation and implantation following pathological processes of the tubes and ovaries.

Cancer of the Esophagus.—A review of 82 cases of cancer of the esophagus and gastric cardia was presented by Prof. José Maria de Freitas and co-workers. The localization of tumor was as follows: interior third plus cardia, 46 cases; inferior third, 17; median third, 12; superior third, 3; and not specified, 4. The outstanding symptoms in these 82 cases consisted of: dysphagia, 69 times; vomiting and regurgitation, 57 times; pain at the inferior third of the retrosternal region, 52 times; and hemorrhage with hematemesis and melena, 10 times. All patients were noted to have lost weight, the loss being more than 10 kg. in the majority of cases.

X-ray examinations of the esophagus and stomach and endoscopic study of the esophagus, larynx, and bronchi are of the utmost importance for the diagnostic confirmation of cancer of the esophagus and cardia and the ultimate indication for surgical therapy. Good results were obtained through endotracheal anesthesia with total curarization, automatic respiration being controlled by the pulmotor; with surgical approach through left thoracotomy with resection of a rib; with esophageal-gastric or esophageal-jejunal anastomosis made with cotton sutures, far apart from each other, in two planes: those of the total inner layer being U-shaped and those of the external layer doubly anchored; systematic use of blood, about 500 cc. at each transfusion, alternating with saline, during the surgical proceedings; closed pleural drainage during 48 hours or more; esophageal-gastric intubation for 48 hours; and systematic use of penicillin and streptomycin locally and parenterally. Feeding is begun early, as soon as the 1st postoperative day, and consists of small amounts of liquid hourly until the 3rd day, reinforced with light foods the 10th postoperative day. Early passive and active exercise soon after the operation and early rising from bed, from the 3rd to the 5th postoperative day, are to be recommended.

The results obtained with surgical treatment (resection of esophagus and cardia) in 39 cases out of the 82 studied were as follows. Two patients who submitted to total resections of the esophagus lived through the immediate postoperative period, as did 19 of the 37 who submitted to transthoracic resection of the esophagus and cardia with immediate anastomosis. Among this same group, 18 died immediately. In the rest of the group, consisting of patients who underwent palliative operations, there were 18 deaths. Two patients died without having been operated on. Causes of death in 19 out of 39 patients who underwent resection were as follows: dehiscence of anastomosis 5, surgical shock 1, postoperative hemorrhage 3, cachexia 6, bronchopneumonia 2, and toxemia 1. The mortality rate tended to diminish in proportion to the speed with which the diagnosis was established and the rate that the authors' experience increased. Two patients underwent total resection of the esophagus six months and three years later, with cervical esophagostomy and gastrostomy, respectively. From those 19 patients who underwent radical operation, 2 persons lived two months, 1 lived three months, and 2 lived six months. This last one has been feeling well and is reasonably well nourished.

ECUADOR

Inquiry into the Health of Apparently Healthy Workers.—The Office of Ecuadorean Social Security, which is charged with giving medical care to private employees and workers, is studying the possibility of initiating services of preventive medicine. For this purpose, an inquiry was made in the city of Guayaquil, under the direction of Dr. Alfredo Valenzuela, into the health of 5,000 employees and workers. The results of this inquiry are interesting, since the employees and workers were apparently healthy.

Of the 5,000 persons examined, 3,317, or 66.34%, were men and 33.66%, women. Their ages varied between 20 and 50 years, but 66% were between 21 and 40 years of age. Seventy-six per cent were public and private employees, and 24% were factory workers. Of all these workers, 71% had a monthly income varying between 200 and 800 sucre, that is, $11 to $46, monthly; it should be noted that the cost of living in this country is somewhat less than that in the United States. Nevertheless, it is evident that the average monthly income is insufficient to satisfy even the most elementary needs.

Intestinal parasites were found in 62.84%, distributed as follows: Trichuris trichiura, 41.32%; Endamoeba coli, 21.08%; Ascaris lumbricoides, 11.68%; Trichomonas intestinalis, 7.60%; Ancylostoma duodenale, 6.36%; E. histolytica, 4.62%; Giardia lamblia, 3.74%; Taenia solium, 3.24%; Strongyloides stercoralis, 2.52%; Hymenolepis nana, 0.5%; with smaller percentages of Chilomastix mesnili, Balantidium coli, Oxyuris, Cercomonas, and Anguillula organisms. In 17.4% two or more of these parasites were found in the feces in association.

In regard to venereal diseases and syphilis, all the women in the inquiry denied ever having suffered such infections. Among the men, 19.54% stated that they had had gonorrhea, and 14%, chancre. Serologic tests in all those suspected and all those who

The items in these letters are contributed by regular correspondents in the various foreign countries.

had had any venereal infection were positive for syphilis in 8.6%, of whom 6.7% were men and 1.9% women.

There were 105 persons, or 2.1%, who proved to be tuberculous; of these, 48 showed slight tuberculosis, 41 moderately advanced tuberculosis, and 16 very advanced tuberculosis. Red blood cell counts between 3,800,000 and 4,200,000 were found in 76%, which indicated moderate anemia. In 11.24% the count was over 4,500,000 and in the remainder less than 3,700,000. Cardiac diseases had a low incidence: 0.88%, consisting, in most cases, of sinus tachycardia (0.36%). Similarly, there was a low incidence of renal diseases, amounting to a total of 0.83%.

Among the other diseases found, the principal ones were as follows: chronic constipation, 36.19% (22.10% in women); acute pharyngitis, 22.79% (women, 13.49%); tonsillitis, 22.21% (women, 15.80%); arterial hypertension, 10.58%; hernias (inguinal, umbilical, and epigastric), 5.49% (women, 2.66%); articular rheumatism, 5.27%; malaria, 3.9%; colitis, 2.76%; bronchial asthma, 2.44%; hepatitis, 2.27%; chronic bronchitis, 1.68%; varices, 1.58% (women, 1.55%); peptic ulcer, 1.28%; hemorrhoids, 0.69%; epilepsy, 0.06%; and cancer of the neck of the uterus, 0.06%. It is interesting to note the present low incidence of malaria, since the campaign carried on systematically throughout the coastal regions, contrasting notably with the figures of 5 or 10 years ago.

Tuberculosis in Azuay.—Under the direction of Dr. Agustín Landivar, the Ecuadorean Antituberculous League has carried out an investigation on the incidence of tuberculous infection and disease in the inhabitants of the central province of Azuay.

The investigation covered 10,734 persons, among whom 7,959 were found positive to the Mantoux test (40.95% with one plus; 37.25% with two; 13.3% with three, and 8.3% with four pluses). Of the total number, 4.66% were found to have active tuberculosis and 0.78%, inactive forms of tuberculosis.

The Rosenthal multipuncture technique was used in vaccinating 2,946 persons; tuberculin allergy and positive reaction to the Mantoux test were found to have been produced in 91.32%.

FINLAND

Bilberry Cure for Oxyuriasis.—The encouraging experiences of a three day bilberry cure for oxyuriasis at the Children's Hospital in Helsingfors are the outcome of observations of an isolated case. It was that of a 10-year-old boy who came to the outpatient department of the hospital suffering from diarrhea. He was told to eat bilberries for a couple of days. On his return to the hospital a fortnight later he had ceased to discharge pinworms (Enterobius vermicularis). This led to an extensive trial of bilberries as a cure for this condition by Dr. Bernhard Landtman of the Children's Hospital. The patients thus treated were 15 boys and 15 girls between the ages of 2 and 15 years. As many as 25 of them had been treated for oxyuriasis by various other means without success. From about half a liter to two liters of bilberries were eaten daily for three consecutive days, either as such or as a purée or thick soup. When fresh bilberries were not in season they were given in dried or preserved form. They were sweetened with sugar, and about a deciliter of milk was given daily with no restriction of the water intake. But no other food was permitted during these three days.

The success of this treatment depended largely on whether the child was treated in the hospital or at home. In the four cases in which the treatment had no effect the children had remained at home, and it is doubtful that the parents followed faithfully the instructions given them. Indeed, one mother admitted that she gave her child ordinary food on the second day of treatment for fear of starvation. In 18 cases the treatment was given in hospital or some other institution. In most of these cases there was an ample discharge of pinworms in the feces as early as the first day of the cure. As many as 20 patients were kept under observation for more than 3 months after the treatment, and the observation periods ranged from 14 days to 5 years. In none of the 26 successfully treated cases could pinworms be found within a few weeks of the completion of the cure, which seemed to be equally effective whether the bilberries were fresh or preserved. The two children who were found to have suffered a relapse nine months after the cure belonged to the same family and probably represented a new infection. No ill effects or complications were observed in connection with this treatment, which, in the opinion of Dr. Landtman, inhibited the development of the eggs of the pinworm as well as expelled the pinworm itself.

Tapeworm Pernicious Anemia.—The prevalence of the tapeworm in Finland has led to much research in this field, and at the Fourth Medical Clinic in Helsingfors, in the charge of Prof. Bertel von Bonsdorff, investigations have recently been carried out concerning the relationship of this parasite to anemia. Von Bonsdorff has shown that the tapeworm, when lodged in the upper sections of the small intestine, is able to prevent the interaction of the extrinsic and intrinsic factors involved in the development of tapeworm pernicious anemia. In cooperation with Dr. R. Gordin he has lately shown that the tapeworm itself absorbs these particular factors. Another investigation has been carried out at the University Hospital in Helsingfors by Dr. Gösta Björkenheim with special reference to the neurological sequels of the pernicious anemia caused by the tapeworm. During the period 1948-1950 he has carried out neurological examinations at various Finnish hospitals of 95 patients between the ages of 11 and 75 who were suffering from this particular form of pernicious anemia. In as many as 75 of these cases there was evidence of some degenerative process in the nervous system.

A close study of these cases showed that in 34 of them the involvement of the nervous system was severe enough to impair capacity for work, the chief cause of this incapacity being ataxia. A reexamination of 80 of these patients from 1 month to 24 months after vermifuge treatment showed that the blood picture had usually become satisfactory. The condition of the nervous system had become worse only in six patients, while the remainder showed improvement or complete recovery. Indeed, the improvement had been so marked in more than half these cases that a neurological examination revealed nothing amiss. In the opinion of Dr. Björkenheim, this satisfactory response to vermifuge treatment depends on the restored ability of the human organism to make proper use of the essential factors in question. The observation that some lesions of the central nervous system are reversible in cases of tapeworm pernicious anemia must, however, be qualified by the admission that certain of these lesions are permanent. Dr. Björkenheim has found that liver preparations and vitamin B_{12} exert a beneficial influence on these neurological manifestations but not more so than vermifuge treatment alone.

Study of Congenital Syphilis.—At the Haga Welander Home for children suffering from congenital syphilis, Dr. Ole Enkvist of Helsingfors has investigated the problem of whether specific treatment of a syphilitic mother during pregnancy affects the prognosis of her offspring. It has been argued that so-called malignant cases of congenital syphilis, refractory to specific treatment, occur as frequently among the children born to mothers given specific treatment during their pregnancy as among the children for whom no specific prenatal treatment has been given. Dr. Enkvist's material concerns 555 children who suffered from congenital syphilis, who were less than 3 years old, and who could be classified in two groups according to whether their mothers had received specific treatment with bismuth and arsphenamine during their pregnancies. In the first group there were 102 children, and in the second 453.

A comparison of 61 children in the first group with 131 in the second with reference to the date at which the first signs of congenital syphilis appeared showed that there was no appreciable difference in this respect between the two groups. But when they were compared with regard to weights at birth, it was found that the group with untreated mothers was considerably lighter in weight. The mortality among the 102 children in the first group was 26%, whereas among the 453 children in the second group it was as high as 36%. Yet another comparison showed that the number of uncomplicated and relatively mild lesions predominated in the first group, whereas visceral syphilis with a definitely and persistently palpable spleen was commoner in the second group. Syphilis of the bony system was also more frequent in the second group. On the other hand, neurosyphilis

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was more frequent in the first group, and this observation is in conformity with the well-established finding that the neurosyphilis of adults occurs more frequently among patients given inadequate treatment than among others given no treatment at all.

Dr. Enkvist concludes that, though specific treatment of the mother during pregnancy may better the prognosis for her syphilitic offspring, the benefits obtained are not as great as expected. The number of the patients in his first group is rather small for a statistical analysis such as this, and it is further impaired, as he points out, by the lack of sufficiently exact data with regard to the treatment each of the expectant mothers received.

ITALY

Medicosurgical Society.—The medicosurgical society of the Romagna region held a meeting on Feb. 10, under the chairmanship of Professor Sighinolfi. Professor Musconi, from Imola, reported two cases of echinococcus cysts of the liver in which clinical, radiological, and laboratory findings led to a wrong diagnosis that could not be rectified during the surgical intervention because the complications that occurred within the cysts (hemorrhagic overflowing in one case and biliary infarction in the other) had greatly altered their anatomic and pathological characteristics. In the first patient the surgical intervention was performed for gastric ulcer and a blood cyst of the liver was found. One year later during a second intervention in the same patient multiple echinococcus cysts were found, one of which was located in the lumen of the common bile duct. In the second patient a large mass beneath the liver was diagnosed clinically as dropsy of the gallbladder, since all symptoms of echinococcus infection were absent and cysts of the gallbladder were not revealed by the roentgenograms. During the operation the cyst was not found; histological examination justified diagnosis of echinococcus cyst. Professor Musconi concluded that diagnosis of echinococcus cyst is very difficult and sometimes impossible in cases of dead cysts in which all clinical symptoms are absent.

Professor Santini, from Ravenna, discussed radiological diagnosis of gastric ulcer. If the anatomic and pathological statistics are compared with the clinical and radiological, it is seen that diagnosis of gastric ulcer is not thought of often considering the frequency of this lesion. Of particular interest in the statistical study is the ratio between the frequencies of gastric ulcer and duodenal ulcer: in this field the disagreement between clinical pathologists and anatomic pathologists is pronounced in that the former support a more frequent occurrence of duodenal ulcers, the latter of gastric ulcers. Discussing the diagnosis of gastric ulcer, Professor Santini pointed out that in about half of the cases classic symptoms permitting a diagnosis based only on anamnestic study are not present. Radiological examination is superior to clinical examination, but many times a gastric ulcer also escapes the radiologist.

The only radiological pathognomonic sign of the gastric lesion is the niche, but indirect signs, such as antral gastritis, incisura of the great curve caused by spasm of the gastric muscles, retraction of the small curve, eccentricity of the pylorus compared with the base of the duodenal bulb, the deviation toward left of the duodenal bulb, and segmentary rigidity, are also valuable. Several technical devices may be used to put in evidence signs of ulcer; in order for the niche to become visible it is necessary that the bright bundle of rays be perpendicular to the diametrical plane of the gastric cylinder passing through the niche. The study of the patient in standing, inclined, and right triclinic position may be advantageous in each particular case. Therefore, Professor Santini concluded that it is impossible to recommend a standard position, but each position should be used according to the zone that is being studied and to the constitutional configuration of the stomach. Trendelenburg's position should not be excluded since it is very useful in those cases in which the cephalic pole of the stomach is being studied. This zone is often overlooked.

Comparing the advantages that may be obtained by means of an examination with small doses and large doses of opaque medium, he observed that the former is useful for revealing modifications of the folds of the mucous membranes but is almost always insufficient to reveal an ulcerous niche. Large doses of opaque medium can penetrate in the ulcerous excavation provided that the level of the meal reaches the ulcer. When it is believed that the ulcer is located in a high position, a second meal of barium may be given, or else the patient may be forced to a voluntary abdominal retraction while the radiographs are taken. By these means ulcers of the superior tract of the small curve are often detected that otherwise would not have been seen.

This technique in examining the digestive tract has been followed for many years at the radiological department of the Ravenna Hospital where about 5,000 patients have been examined from January, 1948, to July, 1950. The results reveal that the number of gastric ulcers is greater than that reported by clinical physicians and also by some radiologists and that, therefore, the ratio between the occurrence of duodenal ulcer and gastric ulcer is smaller than that usually thought of.

Drs. Suzzi Valli and Dominici reported on the first case of autochthonous visceral leishmaniasis that occurred in the Romagna region in 1951 in an adult living in a locality of the Forlì province. The Romagna region is the source of endemic centers of cutaneous leishmaniasis from which the disease is progressively spreading, but up to date no case of the visceral form had been reported.

SWEDEN

New Light on Rickets.—The tendency of modern textbooks to oversimplify the etiology of rickets by tracing this disease solely to the lack of sunlight and vitamin D is challenged by Dr. Gert V. Sydow, who presents an analysis of 64 cases of active rickets observed during a four year period at a hospital in Sundsvall since its children's department was opened in September, 1947. In addition to the 64 active cases there were 14 in which the disease had been arrested. This analysis, published in *Svenska Läkartidningen* for April 10, 1952, shows that there were 21 girls and 43 boys suffering from active rickets. The average age of the girls was much higher than that of the boys when rickets was first diagnosed; before the age of 10 months there were only 3 girls as compared with 31 boys. On the other hand, among the 13 cases of rickets diagnosed after the age of 12 months, there were as many as 8 girls. There was also a sex difference with regard to the incidence of tetany, which affected 21 infants, 17 of whom were boys. Dr. V. Sydow suggests that these sex peculiarities, if confirmed by a larger series and statistical analysis, indicate a genetically determined element in the etiology of rickets. His material also includes cases indicating a hereditary and familial element in the etiology of the disease. Another observation is that the persons with rickets are undersized, a condition again suggesting a congenital factor of a genotypic nature. Dr. V. Sydow is unable to confirm the theory that rickets is a function of growth and that the risk of developing rickets increases with the rate of growth of the child. It should be noted that his diagnosis of rickets depended on radiological examinations of the wrists and on serum analyses.

Alcohol and Venereal Disease.—The committee appointed under government auspices to investigate problems concerned with the control of alcohol in Sweden has made a special study of the connection between alcohol and venereal disease. In cooperation with the public health service, it issued a detailed questionnaire to patients receiving treatment for venereal disease in venereal disease centers and from medical officers of health and private practitioners. The recipients of this questionnaire were asked to fill in data concerning their sex, age, occupation, the date when infection occurred, and the place in which infection occurred, i. e., in a hotel, a cellar, a passage, or out of doors. Further, they were to tell whether there was a permanent or a casual relationship with the partner, and, if the latter, whether it was for payment. Many other points were raised, such as the character of the places of entertainment in which the partners had met, whether appointments had been made by telephone, and whether the partner was a fellow citizen or a foreigner. They

were asked whether one or both partners were under the influence of alcohol at the time and in what form it had been consumed. The veracity with which the questionnaire was answered may have varied somewhat with the sex and occupation of the recipient. For example, the women were apt to be inaccurate over the character of their partnerships, not liking to be classed as prostitutes. As many as 1,413 questionnaires were answered well enough to be suitable for statistical study. Infections received on Saturdays and Sundays were together more numerous than the infections received during all the rest of the week. More than 60% of the men had been infected by casual or occasional partners. This was so for barely 15% of the women; most of the others were infected by more or less permanent partners. Not one woman considered herself a prostitute. Nearly half of the seamen were infected by prostitutes. About four-fifths of the men infected through prostitution were under the influence of alcohol at the time. During casual relationships, more than half of the men were under the influence of alcohol, and 42% of the women with casual partners consumed alcohol at the time. Patients infected abroad more often were under the influence of alcohol at the time than patients infected in Sweden. It was remarkable that the infection rate was so high in places of entertainment in which no alcohol was served. The 15 pages devoted to this discussion contain many tables and diagrams from which the reader can glean information without drawing any cut and dried conclusions as to the exact share taken by alcohol in promoting venereal disease.

Refusal of Physician to Induce Legal Abortions.—Trouble has lately risen over the refusal of a professor in the gynecologic department of the Sabbatsberg Hospital to induce abortions authorized as legally permissible by the authorities. The matter has been given so much prominence in the lay press that the Swedish Medical Association has felt obliged to publish a memorandum on it. It pointed out that it is the duty of every physician to give the advice and treatment that his patient's condition requires and that is in conformity with scientific knowledge and well-tried experience. He may be held responsible when he ignores these considerations, but no Swedish law obliges a physician to carry out any operation on human beings. Legislation provides for the induction of abortion but does not oblige a physician to induce it when he finds abortion unjustifiable. To threaten such a physician with penalties and dismissal from his post for this reason would be to abandon the principles governing the practice of medicine in the Western world. "It is in dictator states that doctors are obliged in the exercise of their profession to act contrary to their scientific and ethical convictions." It is pointed out in this memorandum that the Swedish Medical Association is concerned only with the principles involved and not with any individual case still before the court.

Prophylaxis of Acoustic Trauma.—In the ear department of the Falun Hospital, Dr. Rolf A. Hillesund has compared the effects of various devices for the prevention of acoustic trauma. With the help of audiograms he noted the protective effects of vulcanite earplugs, ordinary cotton wool, and glass fiber wool on 10 persons with normal tympanums. Vulcanite earplugs are not, in his opinion, bearable as a rule for more than a couple of hours in the day, and they seldom fit well. On the other hand, glass fiber wool can be made to fit well in every case, can be used all day with greater comfort than the vulcanite plug, and is quite cheap. With glass fiber wool in both ears, persons with normal hearing can usually catch a speaking voice several meters away. Dr. Hillesund believes that there is little chance of glass fiber wool provoking eczema in the auditory passages. Referring to the problem of acoustic trauma in general, he pointed out that at the present time the best prophylactic measure seems to be the protection of the individual user rather than the provision of machinery for silencing sounds.

The Influence of Climate on Rickets.—At a meeting of the Swedish Medical Society, several speakers dealt with the diagnosis of rickets by radiological examinations. As these are not always available, clinical criteria become more important than ever, and one speaker referred to craniotabes as the most objective physical test or sign of rickets. The same speaker, Dr. Sixten Haraldson, showed what a profound influence climatic conditions in the north of Sweden can have on rickets. The grotesque skeletal deformities portrayed in the textbooks may be rare, but he has seen a score of cases of craniotabes every year at Kiruna, in the far north of Sweden. After the sunless summer of 1949 there were some three score such cases seen. In the far north much of the penetrating effect of the solar rays is lost, and this loss is not sufficiently compensated for by reflection from the snow or by freedom from industrial pollution of the air. The comparatively sunny months of March and April usually have such low temperatures that little of a child's skin can be safely exposed to sunlight out of doors. The midnight sun in the summer is of course not available for the child who is dutifully sent to bed at night. The sunlight of July and August is often wasted because swarms of mosquitoes often render life out of doors quite unbearable. Dr. Haraldson declared rickets to be one of the causes of the defective teeth and delayed dentition often observed in Kiruna. He was in favor of fish-liver oil as a prophylactic, to be administered with special reference to the climatic conditions in the north of Sweden.

SWITZERLAND

Inquiry on Prefrontal Leukotomy.—The periodical *Médecine et Hygiène*, a Swiss medical journal published fortnightly in Geneva, sent a questionnaire to specialists in psychosurgery from America, France, and Switzerland asking them to express their opinions concerning the indications and contraindications of this therapy, the damage it caused to personality, and the medicosurgical problems it entailed. Answers favorable to prefrontal leukotomy included those from Dr. Freeman, professor at the Psychiatric Institute of Washington, who compared psychosurgery to any other surgical operation devoted to alleviating suffering; from Dr. Wertheimer, professor of neurosurgical clinics at the Faculty of Medicine of Lyons (France), who estimated that leukotomy is an efficient therapeutic act in many cases; and from Professor Lhermitte (Paris), Dr. Bersot (Switzerland), secretary of the European Federation for Mental Health, Dr. Cossa (Nice), and Dr. Feuillet (Nancy) who think that frontal leukotomy is the only medical act capable of opening a way of hope to patients who had before an intolerable life.

Professor Morel, head of the university psychiatric clinic of Geneva, and Dr. Baruk, chief of the clinic of Charenton (Paris), were opposed to leukotomy. The former, founding his opinion on histological facts, estimated that the enormous quantity of fibers cut by the surgical section must provoke the secondary degeneration of the cortical neurons afferent to the sectioned fibers; this opinion is not accepted by Wertheimer, who thinks that there is no degeneration, because of the short fibers of association. Baruk considers that leukotomy results in serious damage to the moral personality of schizophrenic patients and would like to see this operation abolished. Other persons, like Dr. Porot (Alger), admit leukotomy but make reservations for its indications.

Opinion was unanimous that leukotomy should be done only after all other treatment has failed. Leukotomy is indicated only in cases having no tendency to spontaneous healing and showing a behavior that is not compatible with any social life or that is dangerous for the patient (suicide).

Most of the authors, even those who are opposed to leukotomy, do not place much emphasis on the postoperative problems of behavior; if the characteristics change, they change in a favorable rather than an unfavorable way.

Concerning the medicolegal aspect, all believed that the decision must be made by the psychiatrist, but with the agreement, if not of the patient, at least of his family or guardian. The legal responsibility of the patient who has undergone leukotomy varies according to his state of mind, established by a survey, as in any other litigious case.

On the whole, in viewing the gravity of the cases undergoing leukotomy, favorable results, even of modest percentage, though they sometimes reach 20 to 30% of schizophrenias (Wertheimer), must be taken in consideration. In the absence of more effective therapy it would not be wise to recommend abolition of prefrontal leukotomy, even if it is yet only a palliative process.

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CORRESPONDENCE

POTENTIAL DANGER OF ISONIAZID RESISTANCE THROUGH FAILURE TO USE MULTIPLE CHEMOTHERAPY IN TREATMENT OF TUBERCULOSIS

To the Editor:—Not since the advent of streptomycin has the medical profession been given an antituberculosis drug with the tremendous therapeutic potentialities of isoniazid. Are these potentialities to be fulfilled, or is isoniazid to become rapidly ineffective owing to the development of bacterial resistance? The answer to this urgent question depends on the attitude of those responsible for its clinical use. Most physicians are already aware of the dangers inherent in the development of isoniazid resistance, but, if a minority is to take the position that bacterial resistance is a laboratory curiosity of no clinical significance, the value of this drug may be greatly lessened. It is a matter of historical record that the wide use of sulfadiazine in naval training centers during World War II eventually resulted in the establishment of streptococcic types resistant to sulfonamides (Epidemiology Unit no. 22: *J. A. M. A.* **129:**921-927 [Dec. 1] 1945). This unfortunate experience in the administration of drugs to relatively segregated groups appears to have been largely forgotten.

While it is true that bacterial resistance to penicillin and sulfonamides in our civilian population has not yet presented serious difficulties, two facts about isoniazid in the treatment of tuberculosis set it apart as a special problem. First, it is significant that patients in tuberculosis hospitals represent segregated groups; furthermore, they have a more or less active chronic disease. Infection with isoniazid resistant strains of extraneous origin may be expected in some hospitals and, later, in the general population. The euphoria and subjective improvement of patients treated with isoniazid will make their control all the more difficult, and the narrow antibacterial specificity of isoniazid will leave secondary infection relatively unchanged.

The second important fact is that isoniazid is the only commercially available chemotherapeutic agent known, other than streptomycin, against which bacteria can develop practically complete resistance in a single step (Szybalski, W., and Bryson, V.: *Am. Rev. Tuberc.* **65:**768-770, 1952). Although this evidence is based on a study of nonpathogenic tubercle bacilli, it has been indicated that human pathogens behave similarly in the development of isoniazid resistance (Middlebrook, G.: *Am. Rev. Tuberc.* **65:**765-767, 1952; Hobby, G., and Lenert, T. F.: *ibid.* **65:**771-774, 1952). Unlike levels of bacterial resistance, the pattern depends on the drug rather than on the species of bacteria (Demerec, M.: *J. Bact.* **56:**63-74, 1948; Bryson, V., and Demerec, M.: *Ann. New York Acad. Sc.* **53:**283-289, 1950). Also, resistance to isoniazid orginates about 1,000 times as rapidly as streptomycin resistance. In terms of mutation rate, an isoniazid resistant bacterial cell will arise on the average in bacterial populations 1,000 times smaller than are required to produce streptomycin resistance. For those who still believe the origin of resistance by mutation rather than by drug contact is an academic hypothesis, the simple isolation of fully isoniazid resistant strains in the complete absence of the drug by the replicate plate method of Lederberg should remove the last vestige of doubt (Szybalski, W., and Bryson, V.: unpublished data). Although reversion to sensitivity through more rapid growth of sensitive mutants may occur in the laboratory following removal of isoniazid from the media, many bacterial generations are required, and there is no assurance that similar reversion will occur in vivo.

In the recent meeting of the National Tuberculosis Association at Boston (May 26-29, 1952) it was reported by attending physicians that extensive tests of isoniazid are in progress or are soon to be made. A few of these tests will contrast the effects of isoniazid used alone against other forms of chemotherapy. This we regard as nothing short of catastrophic. Isoniazid resistant strains of human tubercle bacilli following relatively brief therapy have already been reported by Steenken, Meade, Wolinsky, and Coates (*J. A. M. A.* **149:**187 [May 10] 1952).

When first available, streptomycin was also used alone. The necessity of administering *p*-aminosalicylic acid with streptomycin to retard the origin of resistant strains was learned as a result of much time and effort. When bacterial resistance is a problem, the advantages of using multiple chemotherapy have often been stressed (Carpenter, Bahn, Ackerman, and Stokinger: *Proc. Soc. Exper. Biol. & Med.* **60:**168-171, 1945; Grace, E. J., and Bryson, V.: *Arch. Surg.* **50:**219-222 [April] 1945; Bryson, V., and Grace, E. J.: *New England J. Med.* **237:**683-692, 1947; Klein, M., and Kimmelman, L. J.: *J. Bact.* **54:**363-370, 1947). Mutation to resistance against two drugs used together is theoretically the product of individual mutation rates. In the case of isoniazid and streptomycin combined, a volume of bacteria almost as great as the entire human body would be required for the finding of a cell simultaneously resistant to both agents. On the other hand, the use of drugs in sequence, as resistance develops to each in turn, will not prevent the eventual occurrence of multiple bacterial resistance. If the organisms of human tuberculosis develop very high isoniazid resistance by a single step mutation, no clinically feasible dose of the drug used alone will prevent the selection of resistant strains, providing the bacterial population is moderately large or actively multiplying.

There is no doubt that large-scale tests of isoniazid by hospitals and physicians engaged in private practice will soon begin. In spite of some antagonism of isoniazid with subinhibitory concentrations of streptomycin (Szybalski, W., and Bryson, V.: unpublished data), we suggest most emphatically that isoniazid be employed only in multiple combinations with streptomycin and *p*-aminosalicylic acid or other chemotherapeutic agents active against mycobacteria and not related by cross resistance. For example, streptomycin-*p*-aminosalicylic acid therapy should be compared with and without isoniazid, rather than as an alternative to isoniazid. Otherwise, we predict the early and widespread appearance of isoniazid resistant strains of tubercle bacilli. Such an event will largely neutralize one of the most hopeful developments in the recent history of tuberculosis therapy.

In releasing isoniazid to the medical profession the Food and Drug Administration has approved package labels stating "For use in the treatment of streptomycin resistant tuberculosis under close supervision of a physician." While the treated patient may temporarily improve with isoniazid, the eventual infection of others with organisms resistant to both streptomycin and isoniazid could make any prolonged medical program based on the F. D. A. recommendations a potential threat to the continued value of the drug. We would prefer to see a label stating "For use only in combination with another tuberculostatic drug effective against tubercle bacilli of the patient." The choice may easily be between prolonging the lives of a few desperately ill patients today as opposed to controlling tuberculosis in the United States within one generation.

E. J. GRACE, M.D.
Brooklyn, N. Y.
V. BRYSON, Ph.D.
W. SZYBALSKI, Ph.D.
M. DEMEREC, Ph.D.
Cold Spring Harbor, N. Y.

POLLEN PREVALENCE AND POLLEN-FREE AREAS

To the Editor:—In the correspondence section of THE JOURNAL May 3, 1952, page 82, Dr. Ralph Bookman of Los Angeles voices his concern about the effect on the average physician of my article "Pollen Prevalence and Pollen-Free Areas," which appeared in THE JOURNAL March 1, 1952, page 716. He is also disturbed by the economic and social dislocation which he predicts for many of those pollen sensitive persons "who heed such advice." If this were the first appearance in medical and lay publications of the facts about quantitative pollen distribution, one might be persuaded to share the doctor's pessimism, since no one denies that facts, unless interpreted with common sense, are often dangerous. But the article in question has only augmented a body of similar observations published in numerous medical journals and books over a period of 25 years by many allergists as well as by their collaborators.

It seems pointless to deny that a pollen sufferer may ever escape pollen allergy by avoidance of the pollens to which he is sensitive. This is the only conclusion to be drawn from Dr. Bookman's effort to brand as fallacies first "that it is possible to escape a pollen allergy, and, second, that there are certain areas, suggested by the accompanying maps, to which a pollen sensitive person may flee." In this he does not agree with the teaching of his fellow allergists or take into account the satisfactory experience of many ragweed sensitive patients. Dr. Morrill Wyman, as early as 1876, recorded cases of ragweed allergy in which the sufferer obtained perfect relief for a whole season by going to Europe or to the wooded areas of Canada during August and September. Tuft, in "Clinical Allergy" (Philadelphia, Lea & Febiger, 1949) says, "Complete elimination of the offending allergen from the diet or environment of the patient is the ideal therapeutic method, since it obviates the necessity of other treatment." Feinberg, in "Allergy in Practice" (Chicago, Year Book Publishers, 1946) says, "The ragweed-sensitive patient may be relieved by living in European countries, Asia, parts of South America, Africa, and Australia—no matter what the climate may be. The ragweed-sensitive patient may find increasing relief the farther north he goes into Canada or by going west of the Rockies or to the southernmost portion of Florida. Persons sensitive to certain other pollens may come to the Midwest with consequent relief." Alexander, in "Synopsis of Allergy" (St. Louis, C. V. Mosby Co., 1947) says, "The ideal treatment of hay fever, like other forms of allergy, is to avoid contact with the offending agent. . . . The availability of pollen counts over several years in essentially all sections of the country offers an excellent guide as to where one may go to escape hay fever."

As for Dr. Bookman's statement that "A person sensitized to [illegible]len who moves to this area will probably become sensitized to our local flora within a period of from 6-18 months," the possibility that ragweed sufferers from the middle and eastern states may in time become sensitized to indigenous California pollens has already been discussed in considerable detail by southern California allergists, as well as by those having clinical experience both in the ragweed belt and in southern California (*J. A. M. A.* **139:**554 [Feb. 19] 1949; ibid. **141:**99 [Sept. 3] 1949). Due attention has also been given to the matter in my chapter in Vaughan's "Practice of Allergy," second edition (St. Louis, C. V. Mosby Co., 1948, p. 470). Suffice it to say that there are no published data available on the frequency with which such new sensitization may occur, so that it is not possible to evaluate Dr. Bookman's use of the term "probably" in this connection. It is, however, pertinent to inquire: How many of those who do change residence without any subsequent difficulty take the trouble to report such a happy outcome to any allergist in the new locality?

O. C. DURHAM
Abbott Laboratories
North Chicago, Ill.

ULTRAFILTRABLE ACTH ACTIVITY OF HUMAN PLASMA

To the Editor:—We have previously published in THE JOURNAL (**147:**525 [Sept. 29] 1951) a paper concerning the adrenocorticotropic activity of human blood, directly testing the plasma with the "ascorbic acid depletion method," according to our own technique. In our paper we called attention to the fact that in comparative experiments losses of adrenocorticotropic activity might occur when the determination is made with fractionated plasma (Bornstein and Trewhella, *Lancet* **2:**678, 1950) since the blood fraction with adrenocorticotropin activity is not totally precipitated from +94% acetone.

Our observations and some reports of other authors that the biologic activity of corticotropin (molecular weight 20,000) is not connected with the intact protein molecule but with one of its fractions (Li, C. H.: *Nederl. tijdschr. geneesk.* **94:**1093, 1950) have induced us to investigate whether the corticotropic hormone is, also in the blood, in a form simple enough to be ultrafiltered.

Until now, studies have been performed on blood of five normal adults. The plasma of every person was tested comparatively, before and after ultrafiltration, with the ascorbic acid depletion method. The volume injected in each animal subjected to hypophysectomy was in every case 0.5 cc. per 100 gm. of body weight. Three animals were used for each experiment.

The plasma ultrafiltration was performed immediately, with a cellophane membrane in an adequate ultrafilter, at a pressure of 15 atmospheres, in inert gas (nitrogen) and at a temperature of +2 C. In 90 minutes it is possible to obtain a volume of ultrafiltrate sufficient to make injections in three animals.

Mean falls in ascorbic acid concentration of adrenals expressed as milligrams per 100 gm. of fresh tissue, according to our experimental conditions, were 35.6±3.6 mg. for the plasma before and 46.6±4.25 after ultrafiltration.

From these results, we conclude that the adrenocorticotropic activity of the blood of normal adults is completely ultrafiltrable. Further results on this subject will be published more extensively in another paper.

C. A. ROSSI
L. MONTANARI
M. MARTINELLI
G. MORUZZI
Istituto di Biochimica, Bologna, Italy

CHOLINERGIC DRUGS IN PAROXYSMAL SUPRAVENTRICULAR TACHYCARDIA

To the Editor:—An article entitled "Use of Cholinergic Drugs in Paroxysmal Supraventricular Tachycardia," by Furman and Geiger (*J. A. M. A.* **149:**269 [May 17] 1952) has come to our attention. In the "comment" section of the article by Drs. Furman and Geiger, we note the following statement: "In our opinion, neither agent should be used in the average case except after less dangerous methods have been properly employed without success." Using the word "neither" implies condemnation of both, either individually or in combination. From the studies reported in this paper it is obvious that such a statement indicting either drug independently is not warranted, especially since both had been used in each instance. In the last sentence of the same paragraph we find the statement: "Only in such situations in which the patient's condition is so grave . . . do we feel that the use of methacholine is justified." With the primary attention focused repeatedly on methacholine, neostigmine is still mentioned as an accessory drug of hazardous action.

The undersigned independently introduced the use of neostigmine for paroxysmal tachycardia in clinical medicine in 1941 (*M. Rec.* **153:**134 [Feb. 19] 1941; ibid. **153:**209 [March 19] 1941). In our experience of over 1,000 injections of neostigmine, many of these for supraventricular tachycardia of sinus, auricular, or nodal origin, we have yet to witness a severe reaction due to its use. We still recommend the use of neostigmine methylsulfate, 1 mg. subcutaneously, in the management of paroxysmal supraventricular tachycardia.

SAMUEL WALDMAN, M.D.
1401 President St.
LOUIS PELNER, M.D.
1352 Carroll St.
Brooklyn 13, N. Y.

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COUNCIL ON MEDICAL EDUCATION AND HOSPITALS

The Council on Medical Education and Hospitals has adopted the following statement and voted that it be published.

DONALD G. ANDERSON, M.D., *Secretary.*

FULL COST TUITION

The problem of financing the medical schools, always a difficult one, has been intensified since the end of World War II. To meet this problem, a number of schools have recently considered raising tuition charges to meet or nearly meet the full operating costs involved in the instruction of undergraduate medical students. In support of such action, it is argued that the average medical student will some day receive a comfortable income and that it is reasonable to ask him to pay the entire cost of his education. Several varieties of payment plans with varying exemptions have been suggested, but all are based on essentially the same principle, which is that the medical student, on entering medical school, signs an unsecured note for the difference between the usual tuition fee and the "full cost" to the school of his education, the amount to be repaid over a long period following his entrance into active, private practice. These plans are offered as new and perhaps "revolutionary" innovations in medical school financing. Actually, there is nothing new or unique about them except the techniques of collection.

The principle of full cost tuition is as old as American medical education and was discredited more than 40 years ago. Most of the arguments that may be advanced to support it today were given expression by the proprietary medical schools when an earlier generation of American medical educators stated their conviction that a stable high grade program of medical education could not be financed primarily by student fees. In 1910 Abraham Flexner wrote: "Our conclusion is that established schools . . . may count on fees to the extent of one-third to one-half of the expenditure required to conduct a good school of modern medicine; and that as the department becomes more homogeneously developed, the fees will tend to do even less."

Although the plans referred to assume that a medical school can compute accurately the full cost of educating a medical student, several recent studies have indicated that it is extremely difficult if not impossible for most medical schools to segregate the basic cost of medical instruction from costs incurred in the instruction of other students, in research, and in medical care. Until such figures can be derived, the fairness of any charge that purports to represent the full cost of medical instruction would be open to serious question.

It must be clear that all these plans would be subject to the same dangers and abuses that were inherent in the proprietary schools. It is not unforeseeable that a medical school operating under such a program would be strongly tempted to solve certain of its faculty problems by the simple expedient of raising salaries at student expense. Furthermore, it is but a short step from use of student fees to maintain essential teaching laboratories to the exploitation of such fees for the acquisition of special equipment, for maintaining research, and for the remodeling or even the construction of new facilities. If some of these fears seem farfetched it need only be recalled that they are the very abuses that the leaders of American medicine were struggling but a few years ago to eliminate.

It may be granted that full cost charges would temporarily ease the financial burden of the schools. It is probable, however, that such charges would in time actually make the situation worse. It would mean the abandonment of the established principle that medical education is a social function and is, therefore, rightfully a public trust. Years of effort have been expended in enlisting the interest, sympathy, and support of the general public for medical education, and the splendid development already achieved by the nation's medical schools is a measure of the public's willingness to bear this responsibility. It is entirely possible that placing the whole burden of operating costs on the student might jeopardize or even eliminate other important sources of support by appearing to reduce or to remove the need for support from such sources. Irrespective of the reasons offered in support of such a plan, many will regard the institution of full cost tuition as an abdication of social responsibility by the governing boards of universities.

One of the most serious objections to full cost charges concerns their possible effects on the schools adopting such policies and on the student himself. It is unlikely that a student will either pay these large fees or obligate himself to pay them on long-term contract if he can gain admission to an equally good school at less cost. The full cost school would then be placed at a serious disadvantage in the competition for able students and might easily find itself largely a school of last choice. It is equally possible that many students would choose other careers rather than assume such a long-term financial obligation. The study of medicine would then be left largely to the well-to-do, who could afford outright payment, and medicine would lose the services of many able and deserving persons.

The consequences to the ideals and ethics of medical practice that might follow the practice of putting such a high price on medical education would be most serious. At present, although students of medicine are aware of the financial sacrifice that they make through spending long years in training while their contemporaries are already gainfully employed, they are also aware that others are contributing significantly toward the cost of their education. It is impressed on a student that, while the physician is ordinarily entitled to payment for his services, remuneration must not be the primary consideration on which rendition of service is based. Altruism and compassion are paramount elements and are traditionally considered to be the vital, motivating forces in medical practice. As soon as medical education is placed on a dollar for dollar basis, with a large price attached, those ideals are placed in jeopardy. The graduate, laboring under a large debt, would be sorely tempted to regard his practice as a business enterprise, purchased in the market place, to be exploited and commercialized accordingly.

In view of all these inherent and potential dangers, the Council on Medical Education and Hospitals believes that plans for charging full cost tuition should be condemned as being inimical to the best interests of medical education and the public.[1] It would appear that the future quality of medical schools and of the practice of medicine will be better safeguarded if the medical schools will continue to cultivate and expand accepted sources of support. Recent developments would seem to indicate that there is no need for despair and that, as there is developed an increasing awareness of the social functions and benefits provided by their medical schools, increased support from the general public may be anticipated.

1. The Council distinguishes between plans charging the individual medical student the full cost of his education and plans such as those developed by regional educational programs by which a medical school in one state receives from a governmental agency of another state a subsidy, which may be in the form of a full cost tuition charge, for each student it admits from the latter state. Such a program represents essentially the purchase of services by one state from another state and is not subject to the abuses or undesirable effects that would result from charging the individual student for the full cost of his education.

BUREAU OF MEDICAL ECONOMIC RESEARCH

THE REVISED KEOGH-REED BILLS

(H. R. 8390 and H. R. 8391)

Frank G. Dickinson, Ph.D.

The original bipartisan Keogh-Reed bills (H. R. 4371 and H. R. 4373) were introduced into the House of Representatives on June 7, 1951, at the request of the Special Committee on Retirement Benefits for Lawyers of the American Bar Association. The chairman of the committee is Mr. George Roberts, 40 Wall Street, New York City, and the draftsman of the identical bills was Mr. Leslie R. Rapp, a lawyer of New York City. Late in 1951 Mr. Roberts organized a Co-ordinating Committee on Retirement Benefits for the Professions and the Self-employed and has served as its chairman. This committee is composed of representatives of more than a score of organizations—mostly professional—and of the American Farm Bureau Federation. The representative of the American Medical Association is the Director of the Bureau of Medical Economic Research.

The original Keogh-Reed bills have been studied in great detail by the representatives of many national organizations. Several conferences were held with the technical staff of the Joint Committee on Internal Revenue Taxation of Congress. The revised drafts of these identical bills were introduced on June 27, 1952, by Representatives Eugene Keogh (D, N. Y.) and Daniel Reed (R, N. Y.). (In order for a bill in the House of Representatives to be truly bipartisan, two identical bills must be introduced, one by a Democratic Congressman and the other by a Republican Congressman.) They were referred to the Committee on Ways and Means on June 27, but the committee took no action on them before Congress adjourned on July 7. The bills will be introduced again next January. The revised bills (H. R. 8390 by Mr. Keogh and H. R. 8391 by Mr. Reed) resulted directly from the hearing of May 13 by the Committee on Ways and Means of the House of Representatives.[1] At that hearing, a number of amendments and changes were suggested by some of the 19 persons who testified. In the revised draft an attempt was made to follow as many of the suggestions made during the hearing as seemed to be in the public interest.

The general purpose of this bill is to provide a voluntary pension system for self-employed taxpayers who cannot be covered under the terms of section 165 (a) of the Federal Internal Revenue Code and to cover employed persons who for one reason or another are not covered and cannot expect to receive a pension from their employer. In other words, the purpose of this revised measure is to bring about a degree of equity for the taxpayers who are not now covered by pension plans with those who are now covered by pension plans approved under section 165 (a), by pension plans of local, state, and federal units of government, or by plans of nonprofit organizations. It is imperative that the federal internal revenue law cease to discriminate against certain taxpayers in the matter of pensions.

This discussion is not concerned with the Social Security Act, which for the present purposes may be considered the first layer of pensions; rather it is concerned with the second layer of pensions, in which the employer and employee, by a wide variety of plans, seek to provide pensions for the employees to be financed by premiums paid to insurance companies or by amounts set aside in pension and profit sharing trusts. More than 16,000 pension plans have been approved under section 165 (a) since it was enacted in 1942. Ten million of the 60 million gainfully employed are currently outside the scope of this section because they are self-employed. But the self-employed, as they grow older, are just as much subject to the feebleness and vicissitudes of old age as those who during the working years were employed persons covered by employee-employer pensions.

Before the differences between the old and the new versions of this measure are explained, certain basic facts should be set forth. Although it has not been possible to obtain any data from the pension trust section of the Bureau of Internal Revenue, available estimates indicate that several billion dollars paid by employers into a variety of pension plan funds are not currently being taxed to either the employer or the employee, although the employee when he retires will be required to declare as taxable income that portion of his pension that was financed by his employer. It should be clear, therefore, that this measure does not introduce a new factor into our revenue law but rather permits self-employed taxpayers and employed taxpayers not now covered by pension plans to defer taxes on certain portions of their current income. The setting aside of funds by the self-employed alone under this revised measure might possibly exclude a half-billion dollars annually from current taxation; on this sum, of course, taxes would eventually be payable.[2] The wide support given to the pension plans authorized under section 165 (a) by Congress since 1942 clearly establishes a favorable attitude toward the extension of similar privileges to those taxpayers not now covered. There would be no tax avoidance—only tax deferment. For this reason it would be better to extend our revenue legislation to cover them than to repeal section 165 (a), under which 16,000 pension plans have been approved.

The revisions and changes in this measure have occupied the attention of many persons. The special committee of the American Bar Association on Retirement Benefits for Lawyers has supervised the study and consideration during the past year that culminated in the hearing on May 13. The Bar Association committee was ably assisted by representatives of the American Medical Association, the American Dental Association, the American Institute of Accountants, the American Farm Bureau

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Director, Bureau of Medical Economic Research, American Medical Association.

1. Postponement of Income Tax on Income Set Aside for Retirement, Hearing Before the Committee on Ways and Means, House of Representatives, Eighty-Second Congress, Second Session, on H. R. 4371, H. R. 4373, H. R. 3456, H. R. 1173, H. R. 5847, and H. R. 7426, May 13, 1952, United States Government Printing Office, 1952.

2. Footnote 1, page 47. According to the Treasury Department analysis of the original bill, the maximum conceivable revenue loss would be 3.7 billion dollars. Their statement is that "if 25% of the eligible individuals were to take full advantage of the bill, the current revenue loss would be nearly one billion dollars." If you change the 25% to 10%, which I consider a more reasonable estimate (one-third of the eligible persons excluding, on the average, one-third of the amount excludable = ⅓ × ⅓, or, roughly, 10%), the resulting current revenue loss would be 0.25 billion dollars. If we assume that 50% of my excludable amount of one-half billion dollars would be a loss in current revenue, then the difference between our two estimates is the difference between my 0.25 billion dollars and the 0.37 billion dollars. This is not a great difference, and I feel reasonably sure that their estimate could be lowered to mine, or even below mine, if they were basing it on the self-employed alone, or if they were basing it on the revised bill.

A half-billion dollars is 1.5% of the 36 billion dollar income of the self-employed in 1950. (The maximum excludable is 10%.) Since an unknown portion was a return on investment and, therefore, not earned income as defined in the Keogh-Reed bill, a considerable portion of that income would not be excludable under this bill. On this basis a half-billion dollars would obviously be a very high estimate. In 1950 the average income of the 10 million self-employed was $3,400 as compared with $3,200 for all 60 million gainfully employed. Personal savings for all persons in 1950 were $10.7 billion or 4.8% of total personal income. If the self-employed saved 4.8%, they would have saved not more than $1.8 billion. If they had put one-fourth to one-third of their personal savings into restricted retirement funds authorized by this bill, they would have excluded roughly a half-billion dollars, a high estimate when one considers the unattractiveness of the restricted retirement fund as an investment. Few eligible taxpayers under 40 to 50 years of age would consider it an attractive investment. Certainly most of the personal savings would still be invested in other forms, such as buildings, working capital, government bonds, and stocks.

Employers paid $1.56 billion as payroll taxes under the Social Security Act, as amended, in 1951. This was business expense that will never be taxable to either the employer or the employee. Probably taxes are being deferred on at least twice that sum on account of the payments made by employers to pension plans approved under section 165 (a). Thus, by several methods of estimate, the latter sum will be increased by less than one-sixth on account of exclusions by the self-employed under the Keogh-Reed bill. Further study will be required for an estimate of the amount that would be excluded by the pensionless employed who would be eligible under this bill because their employers do not have pension plans.

To me, the most significant point in the Treasury's analysis of the original Keogh-Reed bill is the last paragraph, which I interpret to mean that the Treasury admits that 10 million self-employed taxpayers are discriminated against by being excluded from section 165 (a) and that the Treasury would remedy this obvious discrimination by repealing section 165 (a), thereby jeopardizing the pension expectations of employees under more than 16,000 approved pension plans.

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Federation, the Author's League of America, the American Federation of Radio Artists, the National Society of Professional Engineers, the Conference of Actuaries in Public Practice, the Association of Stock Exchange Firms, the Society of Industrial Designers, the American Institute of Chemists, the Investment Counsel Association of America, the United Bondholders of America, the American Veterinary Medical Association, the National Federation of Business and Professional Women's Clubs, and many state and local units of these great national organizations, many of whose members are self-employed because of the dictates of custom and law.

The list of changes made by the revised bills follows. No attempt has been made to arrange these changes in order of importance.

1. Several persons who testified on May 13 noted that the original bill provides only one method by which the excludable amounts could be invested, that is, through a trust fund established by ". . . a bona fide agricultural labor, business, industrial or professional association or similar organization for the exclusive benefit of its participating members. . . ." Accordingly, the new draft provides the eligible taxpayer with the option of purchasing a retirement annuity contract from an insurance company, provided the insurance contract contains the same restrictions as the restricted retirement fund. This additional method would avoid forcing any professional man to belong to a professional society as a condition for obtaining benefits under this measure and would, furthermore, give the large life insurance companies an equal opportunity to interest eligible taxpayers in using insurance company annuity contracts as a method of saving for old age. Moreover, the restrictions in this revised measure are so great that the combined efforts of banks, trust, and insurance companies may actually be insufficient to induce large numbers of eligible taxpayers to forego current consumption and save some of their earned income for old age. With more institutions employed in the development of this voluntary pension system, more persons now outside of pension plans will be encouraged—even urged—to set aside for old age some of their earnings during the working years of their lives. During the past 17 years Congress has repeatedly expressed approval of the general objective of inducing more persons to save for their old age. This voluntary pension system would require deliberate family budgeting of such savings.

2. No subject was discussed oftener during the hearing than the limits on the amount excludable annually, which the original bill has set at $7,500 or 10% of earned income, whichever is the lesser. The members of the committee were impressed with the general argument advanced during the hearing of May 13 that these limits were possibly too generous for the young and too severe for those who are now old. Consequently, the revised draft places an over-all lifetime limitation of $150,000 on the excludable amounts, that is, 20 times $7,500. Also, eligible taxpayers now over 55 years of age may exclude more than 10% of their earned income during the period 1953 to 1972.

Since the normal working period of life comprises about 40 years, a lifetime limit of $150,000 means that the maximum amount of $7,500 could be set aside annually every other year, or during half of the traditional 40 working years, by any eligible taxpayer fortunate enough to earn $75,000 in each of those years. For all practical purposes, this would cut the $7,500 in half and permit $3,750 to be excluded in each of the 40 working years, or the equivalent thereof, by this extremely fortunate person. While effectively cutting this annual limit in half, the revised bill still allows some flexibility; moreover, the amount of pension that the man earning $37,500 a year could finance by excluding $3,750 in each of 40 years will, under this new set of limits, be almost as much as the pension that could be financed by a man earning $75,000 a year who would make only 20 maximum payments during his lifetime. Thus, this new set of limits not only effectively reduces the annual limit but gives those who make less than $75,000 a year an advantage by permitting them to exclude 10% of their earned incomes in more years.

There has also been added under the Special Rule a provision for the exclusion of additional amounts by those who are now between 55 and 75 years of age. In many of the 16,000 pension plans approved under section 165 (a), the employer sets aside large sums of money to finance past-service credits for employees who had worked for him for a considerable length of time before the establishment of a pension plan. A practical counterpart for these past-service credits has been provided under the Special Rule, which would be in effect from 1953 to 1972 and would not apply to eligible taxpayers who will attain age 55 after Jan. 1, 1952. It provides that the amount annually excludable between the 55th and 75th birthdays shall be increased by an amount equal to 1% of the taxpayer's earned net income, or $750, whichever is the lesser, multiplied by the number of full years of his age in excess of 55 determined as of Jan. 1, 1952. But his multiple cannot exceed 20, nor can this additional amount be excluded after the taxable year in which the taxpayer attains age 75. Since the youngest eligible taxpayer is now 56 years of age and will attain age 75 in 19 years, it follows that this provision will expire in the calendar year of 1972. A number of tables presented at the hearing indicated that at the premium rates currently being charged by life insurance companies the maximum monthly cash refund annuity starting at age 75 (not at age 65) that could be financed under this Special Rule would be $1,206 a month—for a person now age 59 who would have an earned income of $75,000 in each of his next 17 years. It is hard to imagine such a fortunate person. Since the lifetime limit of $150,000 also applies to eligible persons over age 55 who would come under this Special Rule, the expected monthly pension starting at age 75 for this person now age 59 would be reduced from $1,206 to $1,013 a month.

Now let us turn from the question of limits on the amounts annually excludable from taxable income to the amount of the pension that could be financed. Tables were introduced during the testimony that revealed that very few younger taxpayers under the General Rule could, at present annuity rates, expect to finance a pension of much more than $1,000 a month starting at age 70. As stated before, under the Special Rule almost no one now over age 55 could finance a monthly pension starting at age 75 in excess of $1,000 a month on a cash refund basis. Thus, the revised limitations will prevent any eligible taxpayer from financing a pension of much more than $1,000 a month starting at age 70 or age 75. Testimony was also given indicating that approximately two-thirds of the pension plans approved in recent years under section 165 (a) permitted maximum pensions of more than $1,000 a month—usually starting at age 65, not at age 70 or 75, when the cost is less—and the remaining one-third of the recently approved plans established a maximum of less than $1,000 a month starting at age 65. It was concluded that the monthly pension target of $1,000 a month provided in this revised draft is a very reasonable counterpart of section 165 (a) for the self-employed and those employed not now covered by pension plans.

Simple arithmetic indicates that a pension of $1,000 a month and $12,000 a year is equal to 16% of the $75,000 of earned income a year that would be the minimum amount that a person would have to earn if he made the maximum contribution of $7,500. Do most industrial pension systems allow a maximum pension of more or less than 16% of average earnings? Only 3% of the new pension plans aim as low as a pension of less than 20% of average earnings. The man earning $37,500 could get a pension equal to 32% of his average earnings, and this 32% would be about the highest percentage that anyone could attain under this bill. Hence, by the test of the percentage relationship between the monthly pension and average earnings, this bill is far more restrictive than section 165 (a) in actual practice.

The bill cannot be considered a "rich man's" bill in any sense of that term. If any better set of limitations had been developed, the authors of the bill would not have proposed a lifetime limitation of $150,000 on the amounts excludable from taxable income. The averaging formulas developed under the regulations promulgated under section 165 (a) have prevented discrimination against low-paid employees. But formulas cannot be applied to an individual. The lifetime limitation is merely the best suggested method of providing the counterpart of section 165 (a). There was no necessity for such a limitation in the language of that section, because it applied to groups. Only by examining the limitations in pension plans approved thereunder can the reasonableness of this lifetime limitation be demonstrated.

3. So much for the maximum pension which is highly theoretical because so few persons could earn $75,000 every year for most of their working lifetimes. We now turn to the average pension. Unrefuted testimony supported by elaborate tables was given on May 13 that estimated the average pension a physician, a lawyer, and a dentist could receive under this revised bill on the basis of the Department of Commerce surveys of the incomes of lawyers in 1947, of dentists in 1948, and of physicians in 1949. The average monthly pension on a cash refund basis starting at age 70 for all members of the profession now under 70 years of age would be $208 for physicians, $106 for lawyers, and $140 for dentists. Furthermore, it was estimated that under the Special Rule for those now over age 55 the average monthly pension at age 75—not age 70—would be $131 for physicians, $121 for lawyers, and $72 for dentists. These average amounts of pension for the members of these three professions will give the members of Congress a much clearer idea of the monthly amount of the typical pension under this revised draft than will any consideration of the maximum theoretical pension. Unfortunately, the Committee on Ways and Means was not given any data on May 13 on average expected pensions for the members of other professions and other groups of eligible taxpayers. This was attributed to the unavailability of income surveys of the other professions. The plain fact is that pensions cost a lot of money, and the members of the Committee were more impressed with the estimated average pensions given at the hearing than with the theoretical maximum pensions in weighing the arguments for and against this proposed voluntary pension system. The amounts excludable annually from taxable income when read separately may still seem large to some persons even with the lifetime limitation of $150,000, but anyone who will examine the probable average amount of pensions under this revised draft will not consider the limits too high. Indeed, as time passes it is probable that the limits may need to be raised in order to encourage this group of more than 10 million gainfully employed citizens to provide adequately for their old age out of their own earnings. They have no employer to pay it for them. This bill would encourage citizens to save some of their own money for old age and to pay taxes on those pensions during their old age.

4. So much for maximum pensions and average pensions expected under this revised draft. The vital question regarding this voluntary pension system is neither of these. The vital question is how much of the maximum pension and how much of the average pension would be attributable to the advantage of tax deferment. Each taxpayer is going to pay for these pensions out of his own pocket. No employer, no unit of government is going to pay him one cent for pensions. No one will be credited with additional amounts in his retirement fund when other employees quit or die. The only gift to the taxpayer, the only way in which this bill would encourage the self-employed and those not covered by pension plans to save earnings for old age during their working periods of life is the enticement of paying lower taxes during the retired years on the pensions as they are received than they would have paid on the premiums (excludable amounts) during their working years, that is, the prospect of reducing total lifetime taxes. On the average, no more than one-fifth, or possibly one-fourth, of these pensions could be considered the real benefit being conferred upon the taxpayer by reason of tax deferment. If this estimate may be accepted for the present, the question before Congress is whether such a benefit of one-fifth or one-fourth of these pensions is sufficient to give these citizens who are excluded from section 165 (a) the counterpart of tax deferment benefits that employees are currently obtaining under that section. It must be stressed that the amount of the pension is four or five times the amount of the benefit that this revised bill would confer upon these taxpayers. After 12 months of study there is still reasonable doubt that the true benefits under this revised bill are actually sufficient to provide equality for those outside the scope of section 165 (a).

The term "expected benefits" is used, for no one can predict the level of income tax rates in future years such as 1973 or 1981. Every taxpayer who would exclude sums under this revised bill is gambling with the future of our income tax rates. Presumably, he would pay smaller taxes during his retired years than during his working years. This statement is reasonable if we are thinking about two men in 1952, one of whom is 45 and now at or near the peak of his earning period of life, and the other 75 and probably retired. We must think about future calendar years, for this bill is concerned with persons as they pass through time, and the actual savings in taxes offered by this bill are highly problematical. Income tax rates have moved upward during the last two decades. It is certainly true that if we turn back the pages 15 or 20 years we could find examples of persons who, if this bill had been available to them 15 or 20 years ago and they had set aside sums of money during their working years in the expectation of paying lower taxes during their retired years starting in 1952, would have found that instead of having a tax savings they would have had a tax loss. Who knows the future of income tax rates?

The option of taking the benefits in a lump sum and paying in turn a capital gains tax is provided in section 165 (a). Therefore, it has been provided in this bill. The grave uncertainties about the future level of income tax rates warrant this capital gains option. For that matter, the future level of the capital gains tax rate is also uncertain.

5. In the original bill any taxpayer covered by a pension plan was permitted to exclude under the bill the difference between the limits of (10% and $7,500 described above) and the amount his employer was currently paying into a pension fund approved under section 165 (a). Testimony given at the hearing indicated that such a provision would be extremely difficult to administer. In the first instance, many employers do not actually know how much they are contributing annually to the credit of their younger employees, especially before the time when the employer's contributions are vested in the employee. Many approved pension plans provide that, if the employee does not continue in the service of the employer until retirement, any contributions made by the employer to the credit of the severing employee shall be distributed by formula to the credit of the continuing employees. Thus it would be very difficult for such an employer to determine—even if required to report annually on something like a W-2 form—the current contribution to the pension fund for a named taxpayer. Furthermore, many taxpayers not employed by taxable employers, such as civil servants, firemen, policemen, school teachers and employees of charitable, religious, and scientific organizations, are covered by pension plans that do not need to be approved under section 165 (a). In the interest of simplicity it seems wise to exclude from this revised draft all persons who are covered by any kind of a pension plan, especially the younger employees, who can expect to be covered after completing a specified number of years of service and those who have actually retired and are now receiving pension payments under such plans. It is true that their exclusion will not produce equity in every case, but excluding them seems imperative. There was even some discussion at the hearing of excluding all employed persons and restricting the provisions of this bill to the 10 million self-employed. The authors of the bill did not go that far, because they realized that there are many employed persons, especially those who are employed for short periods of time, who are not now and who probably never will be covered by employer-employee pension plans. Hence the coverage of this revised bill is a compromise between the extremes of covering every taxpayer and covering only the self-employed.

6. There are thousands, perhaps millions of taxpayers who have extreme fluctuations in income. Some of these and other taxpayers might find it impossible to set aside reasonable amounts necessary to finance retirements unless some carry-over provision were developed. Hence an entirely new section was introduced, section (4), which provides for a carry-over of unused exclusions for a period of not more than five years. No additional exclusions from taxable income made under the Special Rule in the revised bill by those now over 55 years of age can be made under the carry-over provision; that is, the carry-over provision applies only to contributions made under the General Rule, most of which will be made by younger persons. The hardship that this carry-over provision is designed to alleviate is found extensively in the entertainment field and among self-employed

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persons engaged in architecture and engineering. This is not to say that there are no other groups that have described their need for this type of provision, which, as noted above, has been carefully limited to a five year period and must function within the limit of $7,500 per year.

7. Last, we shall consider the severe restriction on the distribution of the proceeds of the restricted retirement fund and exactly similar restrictions on the restricted retirement annuity. In simple language, these provisions would prohibit any withdrawal from these savings funds until the taxpayer reached age 65. In the original bill the age was 60; several members of the Committee on Ways and Means indicated a preference for age 65, the retirement age specified in the Social Security Act. This restriction will greatly deter the use of the provisions of this bill and will certainly confine its use to those who sincerely and honestly want to save for old age and for no other reason. Consider a lawyer aged 40 and his wife contemplating setting aside 10% of his earned income under this measure. First, they would have to decide that they did not want to spend the money, as there would be no regular deduction from their monthly pay check by the accounting department of a corporation. Thus the decision to save would have to be made deliberately. Second, they would realize that they could not touch this fund for any of the financial crises that the family might encounter before the husband reached age 65, 25 years hence. Would that seem to you to provide a serious temptation to abuse the privileges provided by this bill? If you will think back over your own lives, you might conclude that you would have preferred paying the income tax currently and then investing the remainder in some fund that you could tap for the ordinary financial crises that your family might encounter, for the ordinary rainy days for which persons have always saved.

Because of the unattractiveness of this investment opportunity, it was provided that, in the event of permanent and total disability continuing for a period of more than three months, the taxpayer would be permitted to make withdrawals from his savings. There are many financial crises in the family other than the disability of the breadwinner, but withdrawals cannot be made in order to meet any of these other types of crises. Time and experience may demonstrate that this restriction is so severe that it will have to be modified to encourage eligible taxpayers to save for old age. It is one of the most important reasons back of the contention that the use of the provisions under this bill will be so limited that the Treasury will have little reason to worry about the loss of current revenue.

There is, of course, the possibility of repealing section 165 (a) in order to provide equity between the persons not covered by the pension plans and those who are covered by pension plans; or, in other words, between those who now enjoy tax deferment privileges in the financing of their pensions and those who do not. But the repeal of section 165 (a) does not seem to merit any serious consideration. The repeal of that section would destroy most of the 16,000 pension plans and darken the future of millions of loyal employees who are confidently expecting pensions under their company pension plans. Such a solution seems cruel. Rather the solution is to provide for the self-employed and those not covered by any kind of pension plan the privileges of tax deferment that persons covered by pension plans enjoy and expect to continue to enjoy.

Our problem is to rectify the error of 1942, the error Congress made in excluding the self-employed from the tax deferment pension benefits of section 165 (a). We have given a cold shoulder to 10,000,000 self-employed persons. Our problem is also to provide reasonable pension opportunities for employed persons not actually covered by pension plans 10 years later. Until we close this gap we shall have failed to complete the new social theory enunciated in 1935 and implemented in 1942. The heart of this new social theory is that pensions are good and that the Federal government should encourage them. All would agree that pensions are good. But many would not want the federal government to encourage pensions. It seems to me, however, that none can disagree that, if the federal government does encourage pensions, it should encourage pensions for all and not merely for those who are employed by employers who have established pension plans.

COUNCIL ON MEDICAL SERVICE

This is the second in a series of studies made by the Committee on Indigent Care of the Council on Medical Service concerning local plans for medical care of the indigent. A general introduction to the series and the first of the Committee's studies (Erie County, New York) appeared in the May 10, 1952, issue of THE JOURNAL, *pages 188-191.*

MEDICAL CARE FOR THE INDIGENT IN MADISON, WISCONSIN

This report is a study of medical care available for indigent and medically indigent residents of the city of Madison in Dane County, Wisconsin. Dane County has a population of approximately 165,000 and is primarily a farming and dairying county, with some small industries. Including the 14,000 students at the University of Wisconsin, 100,000 persons, 61% of the county's population, reside in Madison, the state capitol and county seat and the main business center of the county.

Public assistance is provided on a county-wide basis, but each of Dane County's 60 political subdivisions is responsible for general assistance to its own indigent residents. For this reason, a study of welfare medical care in Madison is considered more practical than a survey of the entire county's programs.

TABLE 1.—*Estimated Average Monthly Coverage, Dane County and Madison, 1951*

	Dane County	Madison
General Assistance (including medically indigent)	377*	230
Public Assistance	3,651	2,227*
Old Age Assistance	2,175	1,327*
Aid to the Blind	66	40*
Aid to Dependent Children	1,370 (600 cases)	823*
Aid to Permanently and Totally Disabled	60	37*

* Estimate, based on percentage of county's population resident in Madison.

ELIGIBLE POPULATION

Residents of Madison are eligible for general assistance medical care when admitted to the welfare department's relief rolls or deemed medically indigent by the department. An average of 230 residents received such aid monthly in 1951.

An estimated 3,651 persons in Dane County received aid monthly from public assistance programs in 1951. In table 1 are given figures on the various types of assistance, with the proportion of the population aided by each program assumed as the same in city and county.

According to the estimate in table 1, approximately 2,457 Madison residents per month, about 2.5% of the city's population, received general or public assistance and were therefore eligible for medical care at public expense in 1951.

ADMINISTRATION

The general assistance program is administered in Madison by the city welfare department, which determines eligibility of both indigent and medically indigent clients. Each client's eligibility is certified monthly. The welfare department is also in charge of planning and authorization of benefits, subject to the approval of the city council, to which the department makes monthly and annual reports. Any appeals by clients are made to Madison's director of welfare.

The public assistance program for all of Dane County is supervised by the Dane County pension department. Eligibility for aid to the blind and aid to the permanently and totally disabled is determined by the state department of public welfare. The county agency determines eligibility for old age assistance and aid to dependent children and is responsible for the planning, authorization, and approval of bills for all public assistance programs. Certification of clients lasts at least a year before a recheck is necessary. The county pension department reports to the county board of supervisors and to the state department of public welfare. Clients may appeal county decisions to the

state authorities, who must, by law, provide a "fair hearing." Both programs provide for control of abuses by patients; for example, a patient who changes physicians too frequently can be required to choose a single physician to treat him for the duration of his illness.

Complaints against physicians are referred to the Dane County Medical Society. The society's medical coordinator reviews complaints concerning fees or refusal to accept welfare cases and can, if necessary, refer the complaint to the society's board of censors for further consideration as to disciplinary action.

SERVICES AVAILABLE

Benefits provided by the general and public assistance programs are sufficiently alike to be discussed jointly in this report. All health services are potentially available to anyone on any of the programs and are generally provided on a "free choice" basis. Each person is treated according to his needs, and the extent and course of treatment is usually decided on by the client's physician. Home and office calls are provided by physicians on a free choice basis. Specialists' care, in or out of the hospital, is provided on referral by the attending physician. The patient may be referred to a specialist or to a group clinic of his choice.

Madison does not have a city or county hospital; as a result, hospitalization, when recommended by a physician, is available on a free choice basis. The patient may be admitted to the hospital without prior authorization from welfare agencies, and has free choice of a physician for in-hospital care. Provisions for a physician's first visit and for hospitalization without prior authorization insure that there will be no time lapse between the request and receipt of most services.

Madison has no public clinics or hospital outpatient clinics except some specialized clinics maintained by the health department. There are approximately 15 private group practice units located in various parts of the city to which welfare clients may go if they wish to do so. Welfare patients are treated by physicians in the same way as private patients. Any recommendations for services or appliances made by the attending physician are authorized. Drugs, as prescribed by the attending physician, are provided by private pharmacies and paid for by the authorizing agency. Home nursing and invalid home care are also available when necessary or advisable.

A person who needs funds because of illness and who is not eligible for either general or public assistance may receive help from the Community Chest agency in Madison. This agency will help pay for both medical care and hospitalization. Patients are usually referred to the Chest agency by the hospitals, so that a double check is obtained as to eligibility and need.

PROVIDERS OF SERVICES

The patient may be treated by any one of the approximately 300 physicians in Madison, except the nonpracticing staff members of the University of Wisconsin Medical School. The physician need not be a member of the Dane County Medical Society to treat welfare patients, and no participation agreement is required. The client has free choice of physician, even during hospitalization, and has free choice of specialist if specialized treatment is advised by the attending physician. Fifteen group practice units in Madison also participate in the program.

Madison's health department operates well-baby, immunization, and chest clinics, which are open to anyone, whether or not referred by a physician. The health department clinics perform no therapy; the chest clinic is diagnostic and performs fluoroscopic examinations. The health department also employs a full-time health educator whose services are available to any agency interested.

All hospitals in Dane County may accept welfare clients. The general hospitals in Madison and the number of beds in each are given in the following tabulation.

Madison General Hospital	177
Methodist Hospital	132
St. Mary's Hospital	230
Wisconsin General Hospital	750

Wisconsin General Hospital is primarily a teaching institution, maintained by the state; however, it will accept welfare patients from any county in Wisconsin. Each county is allotted a quota for the care of public patients at the state hospital, and the cost of care for these patients is shared by the state and the county. When the quota is exhausted, the county assumes full financial responsibility for any additional public patients admitted to the hospital. There are two nursing homes in Madison itself and approximately 11 in the rest of the county. Home nursing is provided on a contract basis by the Visiting Nurse Service in Madison.

PAYMENT FOR SERVICES

Payments to private physicians are made according to a fee schedule developed by the Dane County Medical Society and the city welfare department and accepted by the county pension department for the whole county. Fees are approximately 80% of conservative normal fees and cover all phases of surgery and medicine, including in-hospital physician services.

The fee for home calls is $3.00 during the day and $4.00 after 7 p. m., with a $2.00 fee for each additional patient seen during the visit. Office calls are $2.00 each. The physician is paid for visits to a hospitalized patient at a rate of $2.00 per visit for the first 10 days, $1.00 per visit for the next 20 days, and $1.00 per visit for the first 10 days of each succeeding month. Physicians who treat general assistance patients submit their bills to the city welfare department. The department sends the money for payment to the medical society, which pays the physician according to the fee schedule, less 5% for administrative costs.

Physicians providing care under the aid to dependent children program are paid directly by the county pension department. Old age assistance and aid to the blind clients who require medical care receive an increase in their monthly aid checks and are expected to pay the physician out of this amount; however, when the grant is used up, the pension department pays any further medical costs directly to the physician. There is no supplementary medical budget for aid to the permanently and totally disabled. Clients of this program receive their medical services as general assistance patients, and the service is paid for by the city welfare department.

Pharmacies are paid directly for prescriptions filled for all classifications of welfare clients and hospitals are paid by the welfare agencies according to fixed *per diem* rates.

COSTS AND FINANCIAL SUPPORT

The general assistance program is supported by city tax funds. The state and county governments share the medical costs of public assistance; the state provides 35% of these funds, and the county provides the rest. Indigent persons who have lived in Wisconsin less than one year and need medical assistance receive care at the expense of the state department of public welfare.

All appropriations are made annually. Budgets for general assistance must be approved by the city council and those for public assistance by the county board of supervisors. Supplementary budgets may be submitted if the funds allocated are insufficient. The agencies are required by law to supply adequate funds; the city must bond itself, if necessary, rather than curtail its program.

The cost figures given in table 2 are for the first six months of 1951. Official figures for public assistance expenditures are available for Dane County only; however, Madison has 61% of the county's population, and, for the purposes of this study, city expenditures have been assumed to be approximately in proportion to population. As previously noted, medical care for the permanently and totally disabled is provided from general assistance funds.

TABLE 2.—*Costs of Welfare Programs*

	Dane County	Madison
General Assistance	.....	$ 22,773.45
Public Assistance	$199,896.82	121,937.06 *
Old Age Assistance	149,250.29	91,042.68 *
Aid to the Blind	2,619.25	1,597.74 *
Aid to Dependent Children	48,027.28	29,296.64 *

* Estimate, based on percentage of county's population resident in Madison.

With the estimated figures as a basis, the total amount expended on welfare medical care in Madison during these six months would be approximately $144,710.51, or almost $300,000.00 a year.

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Following are estimates of the average monthly cost of medical care in Madison for each of the four programs and for each eligible client, as well as the monthly cost of some of the major items provided. For the purposes of this tabulation, the 37 clients estimated as eligible for aid to the permanently and totally disabled have been included with those eligible for general assistance.

	G. A.	O. A. A.	A. B.	A. D. C.
Estimated monthly cost.....	$3,795.58	$15,173.78	$266.29	$4,882.77
(Estimated number eligible)..	(267)	(1,327)	(40)	(823)
Cost per eligible person.....	14.22	11.44	6.61	5.93
Physician's care	4.08	2.60	1.38	2.45
Drugs	1.71	1.12	1.53	0.81
Hospitalization	5.37	2.77	0.29	0.91
Nursing home care.....	2.49	4.34	2.64	....

The average cost of medical care per eligible client for Madison's entire welfare program during this period, based on the above figures, was about $9.82 per month.

MEDICAL SOCIETY RELATIONSHIP

The medical coordinator of the Dane County Medical Society occupies a key position in the city and county medical aid program. His duties are "to make certain that the patients, the doctors and the various agencies are mutually satisfied with the services and the allowances" agreed to by the medical society and the welfare agencies. The coordinator, who serves without pay, acts on behalf of the medical society in controlling abuses by physicians, reviewing complaints, and helping to settle disputed fees. He serves as liaison officer between the medical profession and the welfare agencies and, if necessary, may refer cases directly to the society's board of censors. Much of the success of the total program is due to the work of this office.

It is largely through the efforts of the Dane County Medical Society and its coordinator that the patient is assured of completely free choice of a physician not only for home and office but also for hospital care. The fee schedules established by the society and the welfare agencies provide for fair reimbursement for all services provided by the physician, with compensation according to the treatment given.

It is noteworthy that treatment can be provided by any physician in the county and that no participation agreement is required. Thus, the choice of physician is completely free, not even limited to society members, although the society has a major part in the program through the fee schedule and the coordinator and is used by the city welfare department to distribute payments to the individual physicians.

SUMMARY

The medical aid program for recipients of general assistance and public assistance in Madison achieves reasonably complete unity and coordination through the office of the medical coordinator of the Dane County Medical Society. The services offered under the two programs are almost identical, and payments to physicians are in accordance with a fee schedule agreed on by the welfare agencies and the medical profession. The clients of any relief program are eligible for home and office care, hospitalization, home nursing, convalescent care, and prescribed drugs. As a result, relief clients have potentially available to them every medical service provided in the county, and, because the services are the same for all relief groups, there is little incentive to "jump" from one program to another in order to obtain more and different types of medical service.

For those who are unable to meet the qualifications of general or public assistance but who need aid to pay for medical care, the Madison Community Chest agency has a program of financial assistance. Thus, any person in Madison who finds it impossible to provide himself or his family with medical care has some program of assistance to which he may turn.

A number of features of the Madison program are especially noteworthy. A completely free choice of physician, with the same physician caring for the patient over a period of time and when hospitalized, is the best assurance of a good quality of medical care to the indigent. The fact that authorization is not required before a patient calls a physician means that there will be no gap between the request for and receipt of services. In addition, physicians are paid for all services, thus placing the indigent on a par with private patients and eliminating any stigma that might be attached to indigency.

The role of the medical society of Dane County is admirable. It not only negotiates agreements between official agencies and physicians and sees to it that the physicians give service to all indigents under the terms agreed on but it polices its own membership. The only weakness here is that the control of abuses by physicians is vested primarily in one man. At the present time this man handles the position extremely well. His honesty and fortitude of character are especially suited for this responsibility. It would seem, however, that since the medical coordinator's job is such an all-important cog in the machinery his authority should be shared by a committee of no less than three, so that, in the event one person is unable to carry on, the program can be assured of continued strength and continuity of policy.

From the client's standpoint the program is certainly successful in providing complete medical care with a minimum of delay and red tape. The main objective of the program is to render adequate medical care to relief clients, and in this there can be little doubt that Madison has succeeded.

BUREAU OF LEGAL MEDICINE AND LEGISLATION

MEDICOLEGAL ABSTRACTS

Devices: Chiropractor Not "Physician" Under Federal Food and Drug Act.—This was a proceeding by the United States for the condemnation of 22 devices known as Halox Therapeutic Generators. The case was heard in the United States district court, southern district, California.

A Halox Therapeutic Generator is a device for the electrolysis of a sodium chloride solution. It is housed in a leatherette-covered plywood cabinet, its base being approximately 12 in. by 15 in. and its height approximately 12 in. At the front of the cabinet is a control panel. Inside the cabinet there is a glass jar partly filled with a saturated sodium chloride solution into which carbon electrodes extend, and when the generator is in operation electricity is carried to these electrodes. As a result of the electrolysis of the salt solution, chlorine gas is produced. A small electric fan blows a current of air through the jar and out through a rubber hose. Thus a mixture of air and chlorine gas goes into the tube. This mixture is then administered to patients receiving the "chlorine inhalation therapy" by having the patient hold the rubber tube to his nose and inhale.

Administrative regulations issued pursuant to the Federal Food, Drug, and Cosmetic Act exempt from the labeling requirements devices that are delivered to physicians for use in their professional practice, provided information adequate for the use of such a device by the physicians is readily available. All, save 1, of the 22 devices involved in this suit were shipped to W. G. Keys, who held a valid license as a chiropractic physician from the state of California. Keys maintained several offices in Los Angeles County at which these devices were used by him in his practice. The remaining generator was in the possession of another chiropractor, C. J. Henaghan. At the outset, said the court, it is clear that the generators did not bear adequate directions for use. In fact, they bore no directions for use. This was admitted by the claimant who argued that the devices were exempt from such requirement by virtue of having been shipped or delivered to physicians to be dispensed by physicians in their professional practice. It is at once apparent, continued the court, that the claimant can succeed only if a chiropractor is a "physician" within the meaning of the regulations. The regulations define "physician" as "only those physicians, dentists and veterinarians who are licensed by law to administer or apply such drug or device." Thus the persons to whom the devices were shipped must, first of all, be physicians. Only if they are physicians is it necessary to inquire into the matter of their authority to administer or apply the device.

In its broadest sense, said the court, the term "physician" includes anyone exerting a remedial or salutary influence, as a physician of the soul; however, the court did not believe that the term as used in the regulation was intended in the broad sense. In Webster's New International Dictionary, 2nd ed., 1949, one definition of "physician" is: "A person skilled in physic or the art of healing." In the same volume "chiropractic" is defined as "a system for the practice of adjusting the joints, especially of the spine, by hand, for the curing of disease." Thus a chiropractor is one skilled in the art of healing, in a limited manner, although not one skilled in physic, since this latter term refers to the practice of medicine. In Webster's dictionary a second definition of "physician" is: "one duly authorized to treat diseases, especially by medicines; a doctor of medicine; often distinguished from a surgeon." The chiropractic law of California provides in part: ". . . any licensee under this act who uses . . . the term 'physician' . . . or any other letters, prefixes or suffixes, the use of which would indicate that he or she was practicing a profession for which he held no license from the State of California, . . . shall be guilty of a misdemeanor. . . ." It follows, said the court, that one who is licensed to practice chiropractic in the state of California is not a physician by virtue of such license. The record is devoid of any evidence attributing qualifications as physicians to the chiropractors concerned here.

There is, in addition, a more compelling reason for holding that the seized generators were not exempt from the requirement that they bear adequate directions for use. The exemption regulations define a physician as a physician who is "licensed by law to administer or apply" the drug or device in question. Thus, even if the term "physician" is broad enough to include chiropractors, it includes only those chiropractors who are licensed by law to administer or apply the drug or device. The authority of a licensed chiropractor is defined by law which provides: "One form of certificate shall be issued by the board of chiropractic examiners, which said certificate shall be designated 'License to practice chiropractic,' which license shall authorize the holder thereof to practice chiropractic in the State of California as taught in chiropractic schools or colleges; and also, to use all necessary mechanical, and hygienic and sanitary measures incident to the care of the body, but shall not authorize the practice of medicine, surgery, osteopathy, dentistry or optometry, nor the use of any drug or medicine now or hereafter included in materia medica." The scope of this authority, said the trial court, has not been defined by the supreme court of California, but appellate courts of California have had occasion to consider the question. On the basis of their decisions it is clear that a chiropractor licensed by the state of California is not authorized to treat diseases and ailments by mechanical means. As we have seen, the parties are agreed that the generators under seizure were intended for use in the conditions of arthritis, sinusitis, hay fever, and bronchitis. All these conditions are diseases and as such could not be treated by chiropractors by means of the Halox Therapeutic Generator. It follows that the seized generators were not exempted by the regulations, since they were not shipped to physicians who were licensed by law to administer them.

There is yet a third reason, said the trial court, why the seized devices were not exempted by the administrative regulations. Those regulations require that information adequate for the use of such device by physicians be readily available. By affidavit, Dr. Thienes, M.D., chairman of the department of pharmacology at the University of Southern California Medical School, stated that the use of chlorine gas in an effective antiseptic concentration would be too irritating to be withstood by the average person and that concentrations less than this are ineffective for any purpose. He stated that chlorine gas to be safely inhaled for even a short time requires a concentration of less than 10 ppm. The results of tests made by a chemist employed by the Food and Drug Administration indicated that a constant output of such a safe amount was obtained at only two dial settings. Yet nowhere is it shown that directions were available suggesting such dial settings. Furthermore, even at these settings the chlorine output varied throughout a three hour test period. Thus it is clear, the court concluded, that adequate directions were not available for the use of the generators.

Accordingly, the court held that the 22 Halox Therapeutic Generators must be condemned and disposed of by destruction in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act. *United States v. 22 Devices, More or Less, Halox Therapeutic Generator, 98 F. Supp. 914 (1951).*

MEDICAL MOTION PICTURES

The Use of the Microscope: 16 mm., color, sound, showing time 19 minutes. Prepared by Dr. Merrill J. Shepro, University of Illinois. Produced in 1949 by and procurable on rental ($15) or purchase ($175) from Scientific Film Co., 6804 Windsor Ave., Berwyn, Ill.

This is a textbook type film designed for teaching students the correct and efficient manipulation and care of the microscope. It is composed of the following 12 text units: basic parts of the microscope; optical principles; types of microscopes; light source adjustment; adjustment of optics; slide preparation; correct sitting posture; technique of microscopy; oil immersion technique; cleaning of lenses; care of the microscope; and common mistakes of beginners.

In an effort to produce a textbook type of film in 20 minutes time, certain important phases have been omitted, some are incomplete, and others have been unduly emphasized. Since a great deal of the subject matter does not lend itself to the motion picture medium, most of the information presented is contained in the narration. It would therefore be impossible to digest all the material in one showing.

The following demonstrations are well done: method of determining the source of dirt; operation of field and aperture diaphragms; adjustment of the condenser; and adjustment of the intensity and the illuminated area.

In addition to the general criticisms, the specific point of indicating that a beginner should remove the objective while cleaning it can also be criticized. There is also a lack of clear labeling of parts. The photography is good; but the narration is constant and rapid, and the narrator's voice tends to be somewhat monotonous. The film may be of use in stimulating interest in the use of the microscope for the beginner or as a review for the advanced student.

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Transplantation of the Vertical Recti for Lateral Rectus Paralysis: 16 mm., color, silent, showing time 14 minutes. Prepared by Conrad Berens, M.D., and Louis J. Girard, M.D., the Ophthalmological Foundation, New York. Produced in 1951 by the Photography Department of the New York Eye and Ear Infirmary. Procurable on loan or purchase from the Ophthalmological Foundation, Inc., 314 E. 14th St., New York 3.

An operation to provide lateral movement of the eye in the field of operation of a paralyzed lateral rectus muscle is described, and diagnosis of the condition is made by examination and history. The operation consists of recession of the medial rectus about 5 mm., resection of 7 mm. of the lateral rectus, and splitting of the superior and inferior recti tendons from their insertion into the sclera backward 5 to 7 mm. The lateral half of the superior and inferior recti muscles is attached, together with the resected lateral rectus, at the site of the former lateral rectus insertion.

The operation is done in such a manner as to preserve the integrity of Tenon's capsule. The tendons are reattached to the sclera with absorbable sutures, and the conjunctiva is closed with running silk suture. An illustrative patient is a young girl who shows lack of rotation of the left eye in the field of action of the left lateral rectus muscle before operation. Following operation, movement of the eye in this field is adequate and, apparently, conjugate with the right eye.

The film is designed to show operative technique and also to demonstrate the changes in action of the lateral half of the superior and the inferior recti from adduction to abduction. The photography is very well done. The film would be useful in teaching students of ophthalmic surgery and is recommended for residents and ophthalmological societies.

MEDICAL LITERATURE ABSTRACTS

UNITED STATES

A.M.A. Arch. Dermat. and Syphilol., Chicago

65:379-510 (April) 1952

Human Melanogenesis: Tyrosinase Reaction in Pigment Cell Neoplasms, with Particular Reference to Malignant Melanoma: Preliminary Report. T. B. Fitzpatrick.—p. 379.

Stress Studies in Eczema-Asthma-Hay-Fever Diathesis. T. H. Sternberg and M. C. Zimmerman.—p. 392.

Pituitary Adrenocorticotropic Hormone (ACTH) and Cortisone in Diseases of Skin: II. Allergic and Other Dermatoses; Report of 67 Cases. J. G. Hopkins, B. M. Kesten, C. T. Nelson and others.—p. 401.

Acute Forms of Pemphigus. H. E. Michelson.—p. 422.

Chronic Pemphigus Vulgaris. F. E. Senear.—p. 429.

Genetic Aspects of Malignant Melanoma. E. P. Cawley.—p. 440.

Amyloidosis Cutis: Macular Variant. L. L. Palitz and S. Peck.—p. 451.

Localized Acquired Hypertrichosis. A. C. Ressmann and T. Butterworth. —p. 458.

Asterol® Dihydrochloride Therapy of Microsporum Audouini Scalp Infections. W. Snyder.—p. 464.

*Accidental Tattooing of Face Treated by Abrasion with Sandpaper. W. A. Rosenberg.—p. 466.

Linear Unilateral Basal-Cell Nevus with Comedones: Report of Case. R. G. Carney.—p. 471.

Genetic Study of Hereditary Type of Epidermolysis Bullosa Simplex. R. O. Noojin, J. P. Reynolds and W. C. Croom.—p. 477.

Abrasion with Sandpaper in Treatment of Accidental Tattooing.—A truck driver requested treatment for a bluish tattooing of his face, which had been caused about seven months before by an explosion of the gas tank of his truck. There were streaks and discrete bluish pigmented spots and patches on the left side of the face, especially the forehead and the infraorbital region. His co-workers frequently teased him for having a black-and-blue eye. An area about 2.5 cm. in diameter on the left cheek was anesthetized with procaine hydrochloride, and the skin over the area was treated by abrasion with sandpaper, no. 000, until bleeding was profuse. Within 48 hours a crust formed, which fell off in about five days, leaving a smooth pink surface. In about 10 to 14 days the area healed. Similarly involved areas were treated at weekly or biweekly intervals. Two months after the last treatment, examination showed excellent results and no cicatrization.

A.M.A. Arch. Pathology, Chicago

53:281-390 (April) 1952

Arteriosclerosis in Dog: I. Spontaneous Lesions in Aorta and Coronary Arteries. S. Lindsay, I. L. Chaikoff and J. W. Gilmore.—p. 281.

Methylcholanthrene-Induced Tumors in Guinea Pigs with Review of Literature on Tumors Induced with Polycyclic Carcinogenic Hydrocarbons in This Species. W. O. Russell and L. R. Ortega.—p. 301.

Atrophy of Left Lobe of Liver. E. J. Benz, A. H. Baggenstoss and E. E. Wollaeger.—p. 315.

Renal Siderosis in Rabbits Following Injections of Hemoglobin and Organic Iron. D. Bloom, L. H. Westman and J. J. Lalich.—p. 331.

Mobilization of Mucoprotein by Parathyroid Extract. M. B. Engel. —p. 339.

Studies on Hypersensitivity Arteritis in Rabbits: I. Effect of Acute Arteritis on Blood Pressure. II. Observations on Animals Subjected to Numerous Large Injections of Horse Serum. J. L. Orbison.—p. 352.

Study of Death of Irradiated and Nonirradiated Cells by Time-Lapse Cinemicrography. R. Schrek and J. N. Ott Jr.—p. 363.

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Titles marked with an asterisk (*) are abstracted.

American Journal of Medical Sciences, Philadelphia

223:349-468 (April) 1952

*Early Diagnosis of Cancer of Pancreas Based on Clinical and Pathological Study of 100 Autopsied Cases. R. K. Brown, V. Moseley, T. D. Pratt and J. H. Pratt.—p. 349.

Use of Dextran in Treatment of Blood Loss and Shock. J. S. Wilson, E. H. Estes Jr., J. T. Doyle and others.—p. 364.

*Streptomycin Therapy in Pulmonary Tuberculosis: Controlled Study. A. Goldman, B. Friedman and L. Sale Jr.—p. 370.

Comparison of Resting Electrocardiogram, Exercise Electrocardiogram, and Ballistocardiogram During Prolonged Periods of Observation. A. Soffer, P. N. G. Yu, M. A. Epstein and E. S. Olsan.—p. 378.

*Clinical Significance of Small Benign Gastric Ulcer, with Note on Benign Ulcer of Greater Curvature and in Absence of Free Hydrochloric Acid. E. D. Palmer.—p. 386.

Familial Nature of Amino-Aciduria of Wilson's Disease (Hepatolenticular Degeneration). L. L. Uzman and B. Hood.—p. 392.

Hemophilia: Clinical and Laboratory Observations Relative to Diagnosis and Inheritance. A. J. Quick and C. V. Hussey.—p. 401.

Metastatic Carcinoma of Spleen. A. E. Hirst Jr. and W. K. Bullock. —p. 414.

Penicillin and Chloramphenicol in Treatment of Infections Due to Proteus Organisms. B. A. Waisbren and C. Carr.—p. 418.

Plasma Antithrombin Determination: New Test for Cancer of Pancreas Associated with Jaundice. I. Innerfield and A. Angrist.—p. 422.

Survey of Epidemic Typhus Antibody Levels in Bloods of Individuals Born in Eastern and Central Europe and the United States. M. M. Sigel, L. B. Weiss, N. Blumberg and J. C. Doane.—p. 429.

Erythema Nodosum: Survey of Some Recent Literature. H. Beerman. —p. 433.

Industrial Noise: Its Medical, Economic, and Social Aspects. M. S. Fox. —p. 447.

Early Diagnosis of Cancer of Pancreas.—The clinical records of 100 cases of cancer of the pancreas in which necropsy was performed showed that in 55 cases the symptoms or the findings were suggestive of cancer of the pancreas, while in 41 no evidence of pancreatic disease was revealed by the history, physical examination, or laboratory tests at the time of admission to the hospital. In 73 cases necropsy showed that cure was impossible at the time the patient was examined, either because metastases had developed or because the disease had extended locally to such an extent as to be inoperable. The diagnosis of cancer of the pancreas must be made early if surgical intervention is to offer any hope of cure. If pain in any part of the abdomen, either paroxysmal or constant, has developed recently, there has been an unaccountable loss of weight, and the results of physical examination and gastrointestinal roentgen ray studies are negative, a probable diagnosis of cancer of the pancreas is justified. In early cases of cancer of the body and tail there is no diminution of the pancreatic juice, and hence, if the patient is to be saved, the radical operation must be undertaken when only the symptoms mentioned are present. Bulkiness of the stools indicates absence from the intestine of pancreatic juice, as in no other condition are the stools so massive. Visible fat resembling butter or cream on the surface of the stools or in the surrounding fluid is pathognomonic of pancreatic disease. In order to demonstrate this evidence of pancreatic insufficiency the diet should contain a considerable amount of fat. When limited amounts of fat are fed, there is usually no visible fat on the surface of the stool. The presence of fat, fatty acids or soaps gives the feces a clay color, which is not caused by the absence of bile, as is usually thought. The significant finding on microscopic examination is the presence of large numbers of undigested muscle fibers, which may be studied by feeding the patient daily 100 to 150 gm. of finely chopped beef or ham given raw or lightly broiled. The secretin test will demonstrate deficiency of pancreatic juice. Serum lipase and serum diastase tests, although usually negative in cancer of the pancreas, should be employed whenever possible because, if positive, they are diagnostic of pancreatic disease. Contrary to the commonly accepted view, fever and pronounced leukocytosis are often present in advanced cases of cancer of the pancreas. Liver function tests and the demonstration of occult blood in the stools are misleading and needlessly delay operation.

Streptomycin Therapy in Pulmonary Tuberculosis.—Of 85 patients with pulmonary tuberculosis, 42 were treated with streptomycin and 43 served as controls. Each patient in the streptomycin group received 0.1 gm. of the drug per 11 lb. (5 kg.) of body weight daily, with a maximum dose of 1.5 gm. The total daily dose was divided equally and given at eight hour intervals for 91 consecutive days. Follow-up observations were made at 3 month intervals for 12 months. The treated group showed greater improvement with respect to increase in body weight, decrease of fever, and decrease in sputum weight. Roentgenograms revealed definite improvement in the streptomycin-treated group. The proportion of sputum conversions was definitely greater in the streptomycin-treated group. The greatest improvement occurred immediately after three months of streptomycin therapy. Resistance appeared in approximately one-half of the treated patients after three months of streptomycin therapy. At the end of one year all available cultures in the treated group showed drug resistance.

Small Benign Gastric Ulcer.—Of 100 patients with small benign gastric ulcers measuring no more than 1 cm. in diameter, 20 also had a duodenal ulcer and 1 had peptic ulceration in four locations, including the upper gastrointestinal tract. Five patients had two or three gastric ulcers. Achlorhydria was observed in 10 patients, no free acid being demonstrated on at least two occasions following histamine stimulation plus a 12 hour nocturnal continuous drainage. Of nine patients with ulcers of the greater curvature, six had ulcers in the antrum and three in the middle portion. There were two deaths attributable to the lesions, and important complications occurred immediately prior to or during hospitalization in 45, including severe hemorrhage in 30 and perforation in 12. Surgical treatment was required in 21 for reasons other than suspected carcinoma. Small benign ulcers are important clinically because of the danger of serious complications.

American Journal of Psychiatry, New York

108:721-800 (April) 1952. **Partial Index**

Role of Insight in Psychotherapy. J. R. Reid and J. E. Finesinger. —p. 726.
Long-Term Prognosis in Mental Illness: 30-Year Follow-Up of 141 Mental Patients. W. L. Holt Jr. and W. M. Holt.—p. 735.
Inquiry into Eidetic Imagery with Particular Reference to Visual Hallucinations. S. S. Saltzman and S. Machover.—p. 740.
Some Observations on Treatment in Terminal Phases of Hospitalization. H. R. Gilmore.—p. 749.
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Specific Treatment for Neurovegetative Dystonia. F. Cerulli.—p. 779.

American Journal of Surgery, New York

83:489-612 (April) 1952

Proctologic Manifestations of Carcinoma of Prostate. R. J. Jackman and J. R. Anderson.—p. 491.
Oleogranulomas of Rectum: Following Rectal Instillation of Petrolatum or Ointment Containing Petrolatum. D. A. Susnow.—p. 496.
Significance of Uterine Bleeding in Early Pregnancy. A. Culiner.—p. 500.
Ruptured Adnexal Abscess with Generalized Peritonitis. P. Pedowitz and L. B. Felmus.—p. 507.
Further Simplifying Intestinal Intubation: In Vivo and in Vitro Study. M. O. Cantor and E. R. Phelps.—p. 516.
Delay in Diagnosis of Carcinoma of Stomach: Analysis of 104 Cases. D. B. Gray and G. E. Ward.—p. 524.
*Survey of Fires and Explosions in Hospitals of the United States. B. J. Ciliberti and P. M. Wood.—p. 527.
Herniated Lumbar Disc. S. A. Grantham.—p. 531.
Antithrombin Titer in Pancreatic Cyst. I. Innerfield, A. Angrist and J. W. Benjamin.—p. 538.
Plasma Preparation Simplified for Surgical Use. I. M. Tarlov, P. S. Entmacher, R. Day and A. Martin.—p. 544.
New Approach to Problem of Postoperative Pain. A. H. Iason and H. E. Shaftel.—p. 549.

Fires and Explosions in Hospitals.—Investigation of fires and explosions is difficult, since many institutions are reluctant to give information because of legal entanglements and pending court action. However, an effort was made to review as many as possible of such accidents that occurred in hospitals in the 11 year period from 1938 to 1949. This investigation does not include those reported by Greene in 1941. Questionnaires were sent to all hospitals registered with the American Medical Association in 1948. There were 2,285 replies (35.7%) from 6,400 hospitals. In this group 28 fires and 41 explosions in operating rooms were reported. The commonest cause was static electricity (32 cases), while suction pressure machines and cautery apparatus were the second and third commonest causes. Since static electricity caused 32 of 41 explosions, these 32 cases are analyzed. The operating room had no conductive flooring in 24 (75%) of the cases. There was no grounding in 17 (59.3%) cases. In the light of recommended safe practices for operating rooms, these are extremely high percentages. Sparks from a mask as it was removed, woolen blankets, woolen trousers, rubber-soled shoes, silk slips, sponge rubber cushion on anesthetist's stool, and nonconductive linoleum flooring caused some of the explosions. Explosions due to static electricity occurred most frequently during the last and first quarters of the year. It is estimated that about eight explosions per year due to static electricity occur in hospitals in the United States. Conductive flooring, grounding, and proper clothing are still not used in many hospitals, and this situation should be corrected.

Bulletin New York Academy of Medicine, New York

28:197-276 (April) 1952

Role of Connective Tissue in Diseases of Cardiovascular System. P. Klemperer.—p. 204.
Treatment of Bacterial Infections of Heart and Pericardium. T. H. Hunter.—p. 213.
Observations on Rehabilitation of the Neurologically Handicapped. E. B. Schlesinger.—p. 229.
Group Therapy with Epileptic Children and Their Mothers. Z. de Fries and S. Browder.—p. 235.
Medical Management of Acute and Chronic Arterial Occlusion. A. W. Duryee.—p. 241.
*Surgical Therapy of Acute and Chronic Arterial Occlusion. J. W. Lord Jr.—p. 259.

Surgical Therapy of Arterial Occlusion.—The four cases of acute arterial occlusion may be classified as embolic, thrombotic, traumatic, and spasmodic. In the embolic cases, an embolectomy is generally indicated in patients under 50, if they are seen within 10 hours of onset, if the artery obstructed is the aorta, iliac or femoral artery, and if the general condition of the patient is such that an operation is tolerable. Embolectomy is generally contraindicated for emboli of the upper extremity and of the lower extremity from the popliteal artery down. The use of heparin broadens the indications for embolectomy as far as the age and time factors are concerned. The ideal management of the patient with an acute thrombotic occlusion of a main artery is still conservative and nonoperative. For acute arterial occlusion due to trauma, the best period for repair is between two and twelve hours after the accident. Methods available for repair are direct suture, autogenous vein graft, or homologous arterial graft. The spasmodic type of acute arterial occlusion, seen most frequently with massive venous thrombosis of the lower extremity, is handled best by Veal's method of vigorous passive and active exercise of the leg, with elevation. The surgical therapy of chronic arterial occlusion should be limited to selected cases after failure of nonoperative measures. Only sympathectomy seems to have real therapeutic value in properly selected cases. The surgical procedures discussed by the author are (1) the so-called revascularization of the leg by production of a three-limbed arteriovenous fistula; (2) the operation of "scraping" the thrombosed artery; and (3) the resection of a relatively short segment of the thrombosed artery, followed by insertion of an autogenous vein graft to restore blood flow through the main arterial channel. Finally the author describes a new surgical treatment of occlusion of the subclavian or axillary artery that is due to disorders of the shoulder girdle. The operative procedure consists of total subperiosteal resection of the clavicle followed by removal of the periosteum, division of the scalenus anticus muscle, and mobilization of the subclavian artery. Good early results were obtained with this method in eight patients with shoulder girdle syndromes of hyperabduction, scalenus anticus, and costoclavicular, or cervical rib syndromes that had resulted in temporary occlusion or permanent thrombosis of the artery.

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California Medicine, San Francisco

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Surgical Considerations in Diseases of Pancreas. J. A. Morgan, J. D. Briggs and G. A. Stevens.—p. 255.
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Planned Resection of Regional Lymph Nodes in Pneumonectomy for Carcinoma. J. A. Weinberg.—p. 270.
Pulmonary Resection in Tuberculosis. D. J. Dugan.—p. 273.
Hirschsprung's Disease and Congenital Megacolon. E. E. Leon and R. G. Karshner.—p. 276.
Incidence of Splenic Metastasis of Carcinoma. H. L. Abrams.—p. 281.
Trichophyton Tonsurans (Crateriforme) Infection of Scalp. H. Price and D. R. Taylor.—p. 283.
Carcinoma of Ampulla of Vater: Whipple Operation and 10-Year Arrest in Three Cases. L. C. Bennett.—p. 289.
*Culdoscopy. S. T. Lee.—p. 294.

Culdoscopy.—The culdoscope is an instrument for visualization of the female pelvis through the cul-de-sac. It was designed by Decker and Cherry, when attempts to visualize the pelvis through the peritoneoscope were unsatisfactory because of intervening bowel and difficulty in isolating the pelvic organs. A special trocar and cannula are necessary to perforate the cul-de-sac for introduction of the culdoscope. The importance of performing the procedure in the knee-chest position to utilize the negative pressure produced to draw air into the abdomen and thus push the bowel out of the pelvis has been repeatedly stressed by Decker. On the basis of his own experience with culdoscopy in 45 cases, Lee concludes that cul-de-sac puncture for introduction of a culdoscope is easily made with the patient in the knee-chest position. The pelvic organs can be viewed clearly. In all cases in which laparotomy was done after the examination, the culdoscopic diagnosis was confirmed. In no case in which tubal pregnancy was present was the diagnosis missed in culdoscopic examination. Patients were only slightly uncomfortable after the examination. No pelvic peritonitis resulted in any patient, and no pregnant patient aborted as a result of the procedure.

Delaware State Medical Journal, Wilmington

24:59-82 (March) 1952

Diagnosis and Treatment of Coronary Artery Disease by the General Practitioner. A. H. Clagett Jr.—p. 59.
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Proc. Soc. Exper. Biol. & Med., Utica, N. Y.

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*Pulmonary Infarction from Cardiac Catheterization. H. E. J. Houssay, F. W. Haynes and L. Dexter.—p. 444.
*Virulence Enhancing Activities of Aureomycin on Candida Albicans. E. Seligmann.—p. 481.
Protective Role of Pyridoxin Against Toxic Effects of P^{32}. C. Artom, W. E. Cornatzer and G. T. Harrell Jr.—p. 494.
Effect of Antibiotics on Development of Resistance to Hemolytic Streptococcus Infection. R. S. Speck and E. Jawetz.—p. 510.
Effects of Fluoride on Developing Bones in Tissue Culture. G. H. Paff and M. J. Boyd.—p. 518.
Coccidioides Immitis Spherule Antigen in Complement Fixation Test for Experimental Coccidioidomycosis. R. A. Vogel and N. F. Conant.—p. 544.

Pulmonary Infarction Following Cardiac Catheterization.—The major complications of cardiac catheterization are cardiac arrhythmias, which develop largely as a result of introduction of the catheter into the right auricle and ventricle, and thrombosis at the venotomy site that sometimes propagates centrally. To measure the pulmonary "capillary" pressure, Houssay and associates introduced the catheter by the usual fashion into the pulmonary artery and then advanced it further until it was wedged into one of the distal branches of this vessel. In the first 100 cases in which this procedure was employed, no untoward reactions occurred, but in March, 1950, the first of a series of pulmonary infarctions occurred in a patient with mitral stenosis and congestive heart failure. At first, these infarctions occurred only sporadically, but later they occurred with increasing frequency. Between March and November of 1950, only four such infarctions occurred; between November, 1950, and May, 1951, pulmonary infarcts were produced in 15 of 27 patients with mitral stenosis. In no instance did death occur, but many of the patients had a stormy course for several days. The pulmonary infarction occurred from 2½ to 79 hours following wedging of a cardiac catheter into a branch of the pulmonary artery. In other patients without pulmonary congestion, pulmonary infarction did not occur. When the catheters were sterilized by autoclaving instead of by soaking in mercuric oxycyanide, pulmonary infarction did not occur in 20 consecutive patients with either severe mitral stenosis or congestive heart failure. Thus there seems to be no doubt that chemical sterilization of the catheters was responsible for the infarction.

Enhanced Virulence of Candida Albicans by Aureomycin.—The author describes studies of the mechanism of the stimulation of growth and increase in pathogenicity of fungi sometimes observed in patients treated with antibiotics. The strain of Candida employed proved to be nonpathogenic for mice on intraperitoneal injection of large amounts of cells (320 million) in saline. The aureomycin dose of 2 mg. intraperitoneally was also nontoxic. However, when Candida cells were suspended in aureomycin solution (0.1 ml. of cells in 2.4 ml. of aureomycin) and the mixture injected intraperitoneally, 16 of 17 mice died in one experiment and 28 of the 32 died in another. A similar though less pronounced "drug-fungus" effect was observed when aureomycin was given from 24 hours before to 4 hours after Candida inoculation. Aureomycin given 8 to 24 hours after infection was ineffective. The virulence-enhancing activity of aureomycin was destroyed by standing at room temperature or by boiling. No indication of toxin production or biological alteration of Candida was found in vitro. No direct growth-stimulating effect by aureomycin on Candida was observed in cultures. The action in vivo was one of lowering the animal's resistance.

Psychiatric Quarterly, Utica, N. Y.

26:1-176 (Jan.) 1952. **Partial Index**

Interaction of Physiological and Psychological Processes in Adaptation. R. A. Cleghorn.—p. 1.
Free Association, Silence and Multiple Function of Speech. J. A. M. Meerloo.—p. 21.
*Mental Changes Experimentally Produced by L. S. D. (*d*-Lysergic Acid Diethylamide Tartrate). H. J. DeShon, M. Rinkel and H. C. Solomon.—p. 33.
Prefrontal Leukotomy: Clinical Survey of 100 Cases Given Active Retraining Program in a Mental Hospital. M. Klotz, W. P. Ritchie and B. C. Schiele.—p. 54.
Therapeutic Relaxation: Follow-Up Results in Casualties of War. E. Schmidhofer.—p. 73.
Somatic Organization of the Schizophrenic. S. T. Michael.—p. 78.

Production of Mental Changes by *d*-Lysergic Acid Diethylamide Tartrate.—The chemical *d*-lysergic acid diethylamide tartrate (L. S. D.) belongs to the ergonovine group of ergot alkaloids. This paper describes the mental changes produced by *d*-lysergic acid diethylamide tartrate in 17 experiments on 15 volunteers. Besides such subjective symptoms as change in appetite, poor co-ordination, and nausea, changes were observed in thinking and speech, emotion, mood, affect, sensory and time perception, and behavior; there were also morbid ideas and sensory experiences and neurological signs. The reaction occurred in three phases lasting a total of from 12 to 16 hours; in some subjects a fourth phase, lasting one to several days, was seen. The reaction showed some aspects of an exogenous toxic picture. Even more impressive, however, was the simulation of schizophrenic manifestations. Simple schizophrenic and turmoil states were common. Transient paranoid trends were frequent. Schizophrenic

symptoms such as negativism, ambivalence, blocking, and unexplained smiling were observed. Schizoaffective and manic-like states were also encountered. Catharsis was experienced by only one subject. The reaction was not specific, and the extent to which it was dependent on the basic personality of the subject was not determined. The clinical effects imply involvement of the highest centers of the central nervous system and perhaps of lower levels of the nervous system as well. Further study of this drug is indicated because of the remarkable simulation of schizophrenic and affective psychoses on oral administration of a very small amount of this substance.

South Carolina Medical Assn. Journal, Florence

48:57-82 (March) 1952

Tetanus Neonatorum—Report of Case Treated with Mephenesin. R. J Kahaly and J. R. Harvin.—p. 57.
Dissecting Aneurysm of Aorta: Report of Case. R. S. Pollitzer.—p. 59.
Carcinoma of Cervix Uteri. L. L. Hester Jr.—p. 61.

48:83-116 (April) 1952

Emotional Aspects of Pregnancy. K. G. Lawrence.—p. 83.
Basic Facts Concerning Suicide. O. R. Yost.—p. 86.
The Physician and the Atomic Bomb. V. P. Bond, M. C. Fishler and W. H. Sullivan.—p. 93.

Southwestern Medicine, El Paso, Texas

33:117-156 (April) 1952

Role of Dental Pathology in Head and Neck Complaints. M. P. Spearman.—p. 134.
*The "Best" Method of Prostatectomy. H. M. Gibson Jr.—p. 138.

The "Best" Method of Prostatectomy.—Four surgical approaches to the prostate, the suprapubic, transurethral, perineal and retropubic, are described. The disadvantages, results, and special indications for each method are considered. It is apparent that there is no "best" method of prostatectomy. In general, any one of the methods properly carried out will give satisfactory results in most cases. The method selected by the individual surgeon will depend on his training, inclinations, equipment, and hospital facilities. However, in certain cases, the favorite operation of a surgeon will not give the best results; when this happens, he must be able to adapt the one best suited for the patient. It is no longer sufficient for the urological surgeon or the general surgeon who does prostatectomies to know and perform only one method. In order to give the maximum benefit to the patient, he must learn all four methods.

Surgery, St. Louis

31:487-646 (April) 1952

Aortography in Upper Gastrointestinal Hemorrhage: Experimental Study. J. A. Dolphin and B. Williams.—p. 487.
Treatment of Experimental Acute Pancreatitis with Banthine. W. W. Shingleton, W. G. Anlyan and A. K. David Jr.—p. 490.
Serum Amylase Levels in Experimental Pancreatitis. J. R. Thistlethwaite and R. P. Hill.—p. 495.
Renogastroepiploic Anastomosis in Treatment of Portal Hypertension. R. de Britto, O. Vaz, P. Abdalla and R. da Silva.—p. 502.
Experimental Study of Protein and Fat Assimilation After Total Gastrectomy. T. C. Everson.—p. 511.
Effects of Partial Gastrectomy on Canine External Pancreatic Secretion. D. Annis and G. A. Hallenbeck.—p. 517.
*Suppurative Pelvic Thrombophlebitis: IV. Results. Study of 70 Patients Treated by Ligation of Inferior Vena Cava and Ovarian Vessels. C. G. Collins, R. O. Norton, E. W. Nelson and others.—p. 528.
Intussusception in Adults: Report of 15 Cases. C. H. Brown and A. G. Michels.—p. 538.
Conservative Treatment of Acute Form of Sigmoid Volvulus. N. H. Isaacson and D. B. Greer.—p. 544.
*Carcinoma of Thyroid and Nontoxic Nodular Goiter. E. J. Cerise, S. Randall and A. Ochsner.—p. 552.
Suggested Terminology for Ligaments of Groin; Their Clinical and Surgical Application in Repair of Hernias. C. C. Burton.—p. 562.
Squamous-Cell Carcinoma of Floor of the Mouth. W. L. Mattick, D. J. Meehan and J. P. Haberlin.—p. 575.

Ligation of Inferior Vena Cava for Pelvic Thrombophlebitis.—Follow-up studies are reported on 70 patients who had undergone ligation of the inferior vena cava and ovarian vessels for suppurative pelvic thrombophlebitis between Feb. 2, 1942, and January, 1950. Ligation was performed only if the patients had failed to respond to medical therapy or showed evidence of pulmonary infarction and had severe pelvic infection. Sixty-two of the 70 patients survived. All patients who died within one year of operation were considered operative failures, because the authors feel that ligation accomplishes nothing if the patient dies of distant septic metastasis, even though the vena cava and ovarian vessels are successfully ligated. Four of the eight patients who died were operated on from 9 to 21 days following admission to the hospital, and the authors feel that in these death did not result from delay in operating. Varicosities of the abdominal wall, flank, thigh, or legs did not develop in any of the patients. One woman had varicosities of the legs prior to operation, but they were not made worse by ligation of the inferior vena cava and ovarian vessels. Forty-eight of the patients had no edema. Eight patients noticed occasional mild swelling of the feet after they had been up and about for many hours. Six patients noted some swelling of the ankle and lower half of the leg to about the calf except when at complete bed rest. None of these patients were incapacitated. The vascular status of some of the patients was evaluated, and provided evidence that there was adequate compensation for the ligation of the vena cava. Subsequent surgical procedures required by some of the patients disclosed that the operative hazard was not increased. Menstrual or sexual function was not altered by ligation of the inferior vena cava and ovarian vessels. The authors conclude that ligation of the inferior vena cava and ovarian vessels is indicated in patients with suppurative pelvic thrombophlebitis who fail to respond to medical therapy. Ligation can be done at the same time as other surgical interventions.

Carcinoma of Thyroid and Nontoxic Nodular Goiter.—At the Ochsner Clinic 51 proved cases of carcinoma of the thyroid were compared with 529 cases of nontoxic nodular goiter. The incidence of carcinoma discovered at operation was 19.8% in glands with single nodules, and 12.8% in glands with multiple nodules. In the cases of carcinoma, the average interval between discovery of the tumor and institution of definitive treatment was 5.7 years and between the discovery of the tumor and the time the thyroid was first examined by a physician was 2.8 years. The diagnosis of carcinoma was not made clinically in 63.4% of the cases and was not made at operation in 39% of the cases. In the nine cases of "lateral aberrant thyroid" in which the homolateral lobe of the thyroid was removed, the primary carcinoma was found in the lobe in each instance. The admittedly short term follow-up revealed that about 60% of the patients in the present series are apparently well, and about 17% are dead as a result of the neoplasm. The surgical treatment for carcinoma of the thyroid at the Ochsner Clinic is individualized, but generally hemithyroidectomy with removal of the isthmus is performed on patients whose tumor is limited to the thyroid. If the lesion has spread to the cervical nodes, or locally to muscles, or if there is evidence of local recurrence, radical neck dissection is performed. Patients with massive involvement are best treated by removal of as much tissue as possible, decompression of the trachea, tracheotomy, and postoperative roentgen therapy. The authors stress the following points: 1. Carcinoma of the thyroid cannot be diagnosed early by present clinical means. 2. The incidence of carcinoma in both single and multiple nodular goiters is sufficiently high to warrant prophylactic thyroidectomy for all nodular goiters unless a definite surgical contraindication exists. 3. "Lateral aberrant thyroids" are in reality metastases in cervical lymph nodes and should be so treated.

Western J. Surg., Obst. & Gynecology, Portland, Ore.

60:49-92 (Feb.) 1952

Postmenopausal Vaginal Bleeding. E. A. Schumann and R. W. Hyatt.—p. 49.
Modified Vein Stripper. D. K. Crystal and V. K. Hillman.—p. 52.
Bacteriology of Urine in Late Pregnancy and at Delivery in Relation to Puerperal Urinary Tract Infection. R. J. Alesbury.—p. 54.
Injuries to Hand from Broken Porcelain Faucet Handles. J. H. Boyes, and F. C. Melone.—p. 59.
Sidetracking Operation for Extensive Strictures of Common Duct. H. M. Blegen.—p. 65.
Urethral Diverticulum in the Female. C. P. Gray.—p. 68.
Consideration of Wider Removal of Lymphatics with Combined Abdominoperineal Resection of Rectum. J. M. Beal.—p. 70.
Improved Cervical Cap and Sperm Chamber for Artificial Insemination. E. M. Greenberg.—p. 72.
Indications for Radical Neck Dissection. E. B. Speir.—p. 74.

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Acta Tuberculosea Belgica, Brussels

43:1-76 (Feb.) 1952. **Partial Index**

Early Diagnosis of Coxalgia. E. Delcroix.—p. 5.
Results of Streptomycin Treatment of Osseous Tuberculosis. F. Parisel. —p. 14.
Treatment of Primary Tuberculosis Infection with Para-aminosalicylic Acid. R. de Beule.—p. 23.
*Effect of Streptomycin on Tuberculous Lesions of the Lung. P. Golard. —p. 29.

Effect of Streptomycin on Pulmonary Tuberculous Lesions.—Limitation of pulmonary lesions by fibrous walling-off is a histological reaction characteristic of primary infection. Lung specimens from persons with a severe primary infection treated with streptomycin show a somewhat more pronounced tendency toward walling-off, and the caseous foci are not so pronounced as in untreated patients. These changes are the morphological expression of the body's defensive reaction against infection facilitated by the bacteriostatic effect of the antibiotic. Streptomycin seldom arrests a serious primary infection completely. The best indication for streptomycin treatment occurs in recent miliary infection; signs of anatomical cure have been found in patients who died of other causes after having been treated for miliary tuberculosis. Most of the tubercles show hyperplasia of the lymphocytic elements; structural changes also occur in the central epithelioid cells, forming central lacunae that enlarge as a result of giant cell degeneration. Centripetal lymphocytic proliferation gradually fills the lacunae, making the tubercles predominantly lymphoid. The lymphoid tubercle undergoes hyalinization; the cells accompanying it are resorbed, and only nonspecific fibrous formations are left in the place of the initial lesion. Streptomycin accelerates the natural healing process in chronic miliary lesions, reducing the seriousness of the disease and making it susceptible to other methods of treatment. Streptomycin action on bronchial tuberculous lesions is more rapid and intense than on those in the lungs, and its effects vary with the localization of the lesion in the mucosa or the deeper layers of the tissues. Exudative phenomena are favorably influenced; perifocal reactions decrease and limitation of the lesions is accentuated. Streptomycin, however, has little or no effect on caseous nodules. Parietal cleansing, resorption of exudate, and evacuation of casein are the principal advantages of streptomycin in the treatment of cavities; collapse therapy is usually needed to complete the cure. The rapid and frequent appearance of nonspecific cicatrices, rarely seen in the spontaneous development of tuberculosis, is a characteristic effect of streptomycin therapy.

Annals of Rheumatic Diseases, London

11:1-96 (March) 1952

Peri-Arthritis of Shoulder: Studies of Vegetative Function. E. B. Hansen. —p. 2.
Late Results of Gold Treatment in Rheumatoid Arthritis. N. Egelius, N. G. Hävermark and G. Nyström.—p. 17.
Creatine Metabolism in Arthritis. J. E. Dawson and H. B. Salt.—p. 23.
Subfascial Fat Herniation as Cause of Low Back Pain: Differential Diagnosis and Incidence in 302 Cases of Backache. R. Herz.—p. 30.
*Rheumatoid Arthritis of Menopausal Women Treated with Insulin Hypoglycaemias. Z. Z. Godlowski and H. Paterson.—p. 36.
*Familial Incidence of Rheumatoid Arthritis and Acute Rheumatism in 100 Rheumatoid Arthritics. R. W. Barter.—p. 39.
Observations on Use of Thiouracil in Rheumatoid Arthritis. K. A. J. Järvinen.—p. 47.
Heating Knee Joint. H. M. Whyte and S. R. Reader.—p. 54.
Method of Measuring Sweat from Hands: Some Results in Rheumatoid Arthritis. A. Woodmansey.—p. 57.

Insulin Hypoglycemia in Rheumatoid Arthritis.—Several investigators have observed clinical remissions in patients with rheumatoid arthritis after treatment with insulin hypoglycemia. Godlowski and Paterson report studies on 10 women who had had rheumatoid arthritis for from a few months to 18 years. In all of the women the onset was associated with the beginning of menopausal symptoms, and none had had rheumatic fever or rheumatoid arthritis previously. Before, during, and after treatment the body weight, blood picture, and urinary output of 17-ketosteroids, 11-oxycorticoids, creatinine, and uric acid were determined. Insulin hypoglycemia was induced by giving the fasting patient at 8 a. m. a subcutaneous injection of insulin. The doses varied between 20 and 80 units, but were sufficient to produce the clinical symptoms of hypoglycemia. The hypoglycemic attack was interrupted by means of a glassful of sugared water and a meal rich in carbohydrates. The insulin hypoglycemia was repeated daily for from 14 to 28 days. Nine of the 10 patients showed significant improvement during and for some time after treatment, but all relapsed during the succeeding 10 months, and in some the disorder progressed more rapidly than before treatment. Thus insulin hypoglycemia only temporarily retards the course of this type of rheumatoid arthritis.

Familial Incidence of Rheumatoid Arthritis.—The familial incidence of rheumatoid arthritis and acute rheumatism was compared in 100 patients with rheumatoid arthritis and 100 controls. The incidence of these diseases was 5.3% in the families of patients and 2.3% in the families of controls when grandparents, parents, uncles, aunts, brothers, and sisters were included. The incidences were 11% and 4.6% respectively in the two groups when only parents, brothers, and sisters were included. From these figures it was concluded that approximately one-third of patients with rheumatoid arthritis will have a family history of rheumatoid arthritis or acute rheumatism in two or more members (as many as 7 affected members were recorded in one family of 16); approximately one-third will give a history of one affected member; and the remaining one-third will have no relatives with these diseases. It is suggested that there is a tendency toward development of acute rheumatism or rheumatoid arthritis in certain families. This constitutional tendency is discussed in relation to Selye's "general adaptation syndrome" and Kendall's view that a hypersensitivity state may underlie rheumatoid arthritis. As regards the former, certain persons may have a hereditary weakness in their adaptation mechanism; as regards the latter, it is suggested that certain persons may have a constitutional tendency to react to the effects of the products of an antigen-antibody reaction through the medium of the synovial membranes.

British Journal of Ophthalmology, London

36:113-168 (March) 1952. **Partial Index**

Intra-Ocular Acrylic Lenses: Recent Development in Surgery of Cataract. H. Ridley.—p. 113.
Orbital Implants: Review of Results Obtained at the Moorfields Branch of the Moorfields, Westminster and Central Eye Hospital, London. D. P. Choyce.—p. 123.
Phase-Contrast Microscopy of Animal Vitreous Body. B. A. Bembridge, G. N. C. Crawford and A. Pirie.—p. 131.
Nervous Manifestations in Eales's Disease. M. Jefferson and P. C. P. Cloake.—p. 143.

British Journal of Radiology, London

25:169-224 (April) 1952. **Partial Index**

Evaluation of White-Cell Counting in Radiation Protection. A. C. Chamberlain and E. K. Williams.—p. 169.
SYMPOSIUM ON RADIATION GENETICS
Genetic Aspects of Radiation Risks. A. Howard.—p. 177.
Indirect Effects of X Rays on Chromosomes. G. Bonnier.—p. 180.
Cytological and Cytochemical Approach to Understanding of Radiation Damage in Dividing Cells. A. H. Sparrow, M. J. Moses and R. Steele.—p. 182.
*Limit of Renal Tolerance to X-Rays: Investigation into Renal Damage Occurring Following Treatment of Tumours of Testis by Abdominal Baths. P. B. Kunkler, R. F. Farr and R. W. Luxton.—p. 190.
Radiological Investigation of Stomach Changes Following Loud Auditory Stimulus. H. Jungmann and P. Venning.—p. 202.
Intramuscular Pyelography in Children. K. E. Hodge.—p. 209.

Limit of Renal Tolerance to X-Rays.—After orchiectomy has been done for seminoma of the testis, the region of potential metastases includes the aortic iliac and inguinal lymph nodes and the associated lymphatics. In prophylactic treatment of this region x-rays are commonly employed in a dose of from 2,000 to 3,000 r in three to six weeks. If the kidney is included in the field of irradiation, renal damage may occur. This report is based on a study of over 30 cases. Such damage may be unrecognized unless it is specifically looked for. There is usually a latent period of several months before the onset of symptoms, which in the cases here reported averaged eight months. The first complaints were dyspnea on exertion, headache, swelling

of the ankles, and lassitude. On examination pallor was noted. Edema was usually present, but varied in extent and severity. The blood pressure was increased in all cases at some time. In some patients the retinas showed hemorrhages, exudates, and papilledema, and the clinical picture then suggested malignant hypertension. Cardiac enlargement, pulmonary edema, and hepatic enlargement due to congestion were all found in the more advanced cases. Severe dyspnea was a troublesome symptom. Anemia usually progressed rapidly. All patients had albuminuria, and in the urine of some granular and hyaline casts were found. Some of the patients died within a few months of the onset of symptoms, death being due to chronic uremia or to left ventricular failure. However, considerable improvement was possible even in severe cases following judicious blood transfusions and prolonged rest. Those who survived the initial more acute symptoms had signs of chronic nephritis, such as albuminuria, hypertension, anemia, increased blood urea levels, and impaired renal function. The various techniques that were employed for the prophylactic roentgen irradiation of these patients had been described previously, but in this paper an account is given of the arrangement of the fields and the basis on which the dosage is calculated. The survival rates in 93 cases and the incidence of renal failure are correlated with the distribution of the dose through the kidneys. In patients in whom renal failure developed, one entire kidney or both kidneys had received a dose of 2,000 r or over in five weeks. The "safer" techniques were characterized by smaller doses to the upper poles of both kidneys. The risk of renal failure may best be minimized by insuring that about one-third of the volume of the kidneys is outside the irradiated fields or is irradiated with as small a dose as possible. Renal function and location should be determined before roentgen treatment of the abdomen is undertaken.

British Journal of Venereal Diseases, London

28:1-48 (March) 1952

Interpretation of Serum Reactions in Late Syphilis. C. P. Heywood. —p. 3.
Note on Patterns of Quantitative Serological Tests in Late Syphilis. A. Redmond, C. S. Nicol and R. A. Shooter.—p. 13.
Comparative Serum Testing with Cardiolipin and Crude Heart Extract Wassermann Antigens. I. N. O. Price and A. E. Wilkinson.—p. 16.
Two Cases of Gummatous Ulceration Treated with Terramycin. R. R. Willcox.—p. 20.
Occurence of Neisseria Other Than Gonococcus in Genital Tract. A. E. Wilkinson.—p. 24.

Canadian Medical Association Journal, Montreal

66:309-418 (April) 1952

Acute Pulmonary Oedema. L. C. Steeves.—p. 309.
*Cortisone in Asthma. H. S. Mitchell and G. Cameron.—p. 313.
Early Ambulation Following Abortion. M. M. Davis.—p. 317.
Further Study of Blood Cholesterol in Schizophrenia. G. Nadeau and G. H. Larue.—p. 320.
Syphilitic Cardiovascular Disease. C. L. Hunt.—p. 324.
Common Pitfalls in Medical Practice. G. A. Copping.—p. 329.
Presence of Q Fever Complement Fixing Antibodies in Sera of Inhabitants of the Province of Quebec. V. Pavilanis, P. Lépine and N. Morisset.—p. 333.
Islet Cell Tumours of Pancreas. A. O. Whipple.—p. 334.
Therapeutic Evaluation of Cortisone Applied Topically in Ophthalmic Diseases. J. F. Minnes.—p. 342.
Observations on Physiological Effects of Cortisone and ACTH. H. S. Robinson, R. A. Palmer, A. W. Bagnall and H. W. McIntosh.—p. 347.
*Further Experiences with Para-Aminosalicylic Acid. H. M. Ross.—p. 353.
Management of Erythroblastosis Fetalis. C. E. Snelling, W. L. Donohue and M. McKee.—p. 356.
Investigation of Histoaminolytic Activity of Serum in Pregnancy. W. H. Allemang.—p. 359.
Tuberculous Empyema Complicating Artificial Pneumothorax. H. J. A. Cranz.—p. 363.
Glucose Metabolism in Anxiety States. L. J. Cera, I. J. Matas and F. D. White.—p. 366.
ACTH in Aspiration of Peanuts. M. K. MacGougan and S. B. Thorson. —p. 371.

Cortisone in Asthma.—Mitchell and Cameron studied 21 patients with intrinsic bronchial asthma who had been given courses of cortisone or cortisone and corticotropin combined. The duration of asthma varied from a few months to 49 years; four patients had had attacks for less than two years. The severity of the asthma varied from case to case, but in most cases it was of the severe intractable type, with decreasing response to bronchodilators. Seventeen of the patients were given cortisone by the intramuscular or oral route; two were given corticotropin for the first two days in conjunction with cortisone therapy; one was given corticotropin after several days of cortisone therapy while the cortisone dosage was gradually decreased, and one was given corticotropin after an initial unsatisfactory trial of cortisone. The authors gained the impression that cortisone has a definite role in treatment of patients with intrinsic bronchial asthma whose emphysema is not severe enough to cause irreversible changes in their lung fields. It may be a life-saving measure in patients in status asthmaticus who do not respond to bronchodilators; this is demonstrated in the three cases. The response to the drug is more or less unpredictable. Many more cases should be studied before its value in asthma can be assessed. Cortisone was found to be just as effective orally as intramuscularly. Oral doses of 200 mg. for one day, and then 100 mg. daily for several days thereafter were sufficient. Relapse usually occurred from one week to three months after cortisone had been discontinued. Maintenance doses have to be continued. Cortisone should only be tried in patients in whom all other forms of medication have failed. Side-effects were not frequent. One patient has been taking cortisone for 10 months without ill effect.

Experiences with Para-Aminosalicylic Acid.—The combined use of *p*-aminosalicylic acid orally and streptomycin intramuscularly in patients with pulmonary tuberculosis has become standard practice. In this study one group of 221 patients received only 1 gm. of streptomycin daily for from 60 to 90 days. Organisms persisted in 154 of this number, and in 67% the bacilli showed increased resistance. In a second group 58 patients received 1 gm. of streptomycin and 2 gm. of *p*-aminosalicylic acid daily for the same period. Orangisms persisted in 30 patients, and 64% of these after cessation of therapy had organisms with increased resistance to streptomycin. A third group of 146 patients received 1 gm of streptomycin and 10 gm. of *p*-aminosalicylic acid daily for 60 to 90 days. In 72 cases organisms persisted and 18% of these patients had organisms with increased streptomycin resistance. Thus it would seem that a daily dose of 10 gm. of *p*-aminosalicylic acid rather than 2 gm. along with 1 gm. per day of streptomycin caused a marked reduction in the number of streptomycin-resistant strains of tubercle bacilli.

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Clinica Pediatrica, Bologna

34:1-70 (Jan.) 1952

Studies on Action of Antireticular Cytotoxic Serum in Immature and Dystrophic Patients. G. Brogi and M. Verrotti.—p. 1.
Electrocardiograms in Acute Phase of Poliomyelitis. L. Salmi and M. Malossi.—p. 17.
Effectiveness of Early Introduction of Structural Compounds with Lipotropic Activity in Newborn with Extensive Skin Manifestations of Exudative Diathesis. M. Orlandelli.—p. 29.
*Spinal Block During Streptomycin Therapy of Tuberculous Meningitis. P. Nicolaj.—p. 39.

Spinal Block in Streptomycin Therapy of Tuberculous Meningitis.—A severe complication that may occur during streptomycin therapy of tuberculous meningitis is spinal block. This may occur when the streptomycin dosage is inadequate or it is given only intramuscularly thus inhibiting but not stopping the process, whose slow development leads to spinal block. It may be attributable to local irritation resulting from excess streptomycin administered intrathecally, predisposition of the patient to this complication, or a general allergic reaction to the antibiotic. In patients who were never treated with the drug spinal block may arise either because the process develops slowly, or because the meningeal exudate concentrates around the first part of the spinal cord, obstructing the circulation of the fluid. The author reports on 12 patients, in three of whom spinal block developed before treatment was instituted. In four it resulted from inadequate streptomycin therapy, in four from local irritation by the antibiotic, and in one as a part of a general allergic reaction to the antibiotic after recovery from meningitis. It was more frequent in adults than in children, and as a rule, symptoms were severer in patients who had not received streptomycin or only inadequate doses of it. The spinal fluid in all patients was xanthochromic and showed excess albumin. Six patients died, including all four in whom streptomycin therapy had been

inadequate. It is suggested that the prognosis is more favorable in patients who are not treated with streptomycin before the onset of the spinal block and in those in whom the block was caused by local irritation from the antibiotic. If therapy, which must be individualized, is adequate, the spinal block may recede completely, as in some of the author's patients, with complete restoration of all the functions that had been impaired.

Lancet, London

1:679-728 (April 5) 1952

Factors Which Influence Value of Radiological Investigation. J. F. Brailsford.—p. 679.
*Self-Demand Feeding in a Maternity Unit. R. S. Illingworth, D. G. H. Stone, G. H. Jowett and J. F. Scott.—p. 683.
Sickle-Cell Anomaly as Sign of Mediterranean Anaemia. J. Caminopetros. —p. 687.
Hyperthyroidism and Peptic Ulcer. A. M. Gill and F. W. Walton. —p. 693.
Familial Cataract and Mental Deficiency. B. H. Kirman.—p. 694.
Ornithosis: Isolation of Virus from a Case. P. R. Duncan, A. E. Thomas and J. O'H. Tobin.—p. 696.
Estimation of Formaldehydogenic Steroids. A. A. Henly and M. Potter. —p. 697.
Pituitary Tuberculoma. L. C. Oliver.—p. 698.

Self-Demand Feeding in a Maternity Unit.—A flexible feeding schedule favors the development and maintenance of successful lactation. Babies have been shown to demand very frequent feedings from the fifth to the eighth day of life; when they are kept waiting on a rigid schedule they are apt to become tired and to swallow air as a result of crying, making suckling difficult. The relation of the feeding schedule to the establishment of lactation was studied by feeding one group of 106 babies on a rigid schedule and another group of 131 on a self-demand schedule, beginning on the third day, and comparing the two groups in regard to weight gain, incidence of overdistention of the breasts in the mothers, and incidence of breast-feeding on discharge and at the age of one month. All babies were fed at six hour intervals during the first two days for fear that more frequent feeding might cause soreness of the nipples. Then babies in the demand group were fed when they wanted it, day or night; the others were fed every four hours by day and once at night (6 feedings in 24 hours). Demands from babies in the demand group were most frequent between the fourth and seventh days, 36 babies demanding 8 feedings or more on the fifth day, and 12 demanding 9 or more. Babies fed on demand gained weight more rapidly than the others; by the ninth day 49.1% had regained their birth weight as compared with 36.1% of those on the rigid schedule. Test feedings, showing a positive correlation between the weight gain and the amount of milk taken, indicated that babies fed on demand empty the breast better than those on a rigid schedule. Overdistention of the breast and soreness of the nipples was more than twice as frequent among mothers of babies on a rigid schedule as among mothers of babies in the demand group. The number of fully breast-fed babies in the rigid group declined from 88.1% at the time of discharge to 64.5% at the age of 1 month. Comparable figures for the demand group were 94.4% on discharge and 80.3% at 1 month. Self-demand breast-feeding, by causing better emptying of the breast and less frequent soreness of the nipples, favors lactation.

Nederlandsch Tijdschrift v. Geneeskunde, Amsterdam

96:593-660 (March 15) 1952. **Partial Index**

*Decreasing Mortality from Whooping Cough in Nursing Infants. J. E. Minkenhof and M. W. van der Kooi.—p. 598.
Treatment of Severe Uremia by Intestinal Dialysis and Feeding Through a Cardiac Catheter. G. Bossinga and E. E. Twiss.—p. 604.
*Copper in Treatment of Hypochromic Anemia Refractory to Iron. S. I. de Vries.—p. 611.

Decreasing Mortality from Whooping Cough in Nursing Infants.—Minkenhof and van der Kooi gained the impression that during the last 50 years infant mortality from whooping cough has decreased not only as the result of more spontaneous recoveries but also because of more effective treatment of secondary pneumonia. Furthermore chloramphenicol and aureomycin do not influence uncomplicated whooping cough favorably. On the contrary, they found that in some cases these drugs render other bacteria, such as those causing pyoderma, resistant to all chemotherapeutic and antibiotic drugs. However, secondary bronchopneumonia that has proved resistant to sulfonamides, penicillin, and streptomycin responds favorably to these drugs. Investigating the deaths among 249 infants with whooping cough who had not been immunized against this disease, the authors found that while in 1946 there were 22 fatalities among 56 cases, there were none among 40 in 1951. Secondary pneumonia was treated with sulfonamides or dihydrostreptomycin. Aureomycin was used and proved effective in only two resistant cases. Since 1948, infants with whooping cough have been given dihydrostreptomycin in order to prevent pneumonia.

Copper in Treatment of Hypochromic Anemia.—De Vries reviews the literature on the use of copper in the treatment of anemia. On the basis of his own observations on eight patients, of which four are reported in detail, he is convinced that, in patients with hypochromic anemia who are refractory to treatment with iron and in whom the copper content of the serum is low, treatment with copper will have a therapeutic effect. It is assumed that copper has a catalytic effect in these cases.

Practitioner, London

168:313-448 (April) 1952. **Partial Index**

Cardiac Emergencies in General Practice. C. J. Gavey.—p. 317.
Respiratory Emergencies. N. L. Rusby.—p. 325.
Abdominal Emergencies. R. M. Walker.—p. 331.
Paediatric Emergencies. R. W. B. Ellis.—p. 338.
Obstetrical Emergencies. H. H. Evers.—p. 347.
Neurological Emergencies. E. C. O. Jewesbury.—p. 357.
Psychiatric Emergencies in General Practice. E. W. Anderson.—p. 363.

Ugeskrift for Laeger, Copenhagen

114:351-384 (March 20) 1952

*Simmond's Syndrome Treated with Desoxycorticosterone Acetate, Testosterone Propionate and Thyroidin and with ACTH. H. Petersen. —p. 351.
*Vitamin B_{12} Treatment of Megalocytic and Macrocytic Anemia. J. S. Baastrup.—p. 356.

Treatment of Simmond's Syndrome.—Simmond's syndrome must be differentiated from myxedema, Addison's disease, and anorexia nervosa; myxedema is the most frequent mistaken diagnosis. In the first case reported no treatment was attempted because of the unfavorable prognosis. In one of the three patients treated with desoxycorticosterone acetate (percorten®), testosterone propionate (perandren®) and iodothyrin ("thyroidin") the result was particularly good and in another case the results were good from the somatic viewpoint, but the psychic changes were not affected. During this treatment attention must be directed to such symptoms of overdosage as increase in weight, increase in blood pressure, edema, and signs of cardiac insufficiency. In the cases described slight signs of overdosage were seen in the form of crural edema, increased weight, and increased blood pressure. In the third case in which the combined treatment was used unsuccessfully, treatment with corticotropin (ACTH) had had no effect. The commonest causal factors in Simmond's syndrome were represented, craniopharyngeoma in one case, grave postpartum hemorrhage in two cases; the etiology in the remaining case is unknown. Petersen's impression is that possibly psychic changes cannot be influenced favorably by treatment.

Vitamin B_{12} Treatment of Megalocytic and Macrocytic Anemia.—Seven cases of pernicious and related anemia were treated by intramuscular injection of vitamin B_{12}. In one case of pernicious anemia, one case resembling pernicious anemia, and two cases of macrocytic anemia complete remission resulted, while in two cases of pernicious anemia and one case resembling pernicious anemia the hemoglobin level and the erythrocyte count rose only to slightly subnormal values. Since injection treatment with vitamin B_{12} is agreeable for the patient and since in some cases complete remission follows and in other cases the treatment at least to begin with is as effective as treatment with liver and stomach preparations, it seems to Baastrup reasonable at present first to try treatment with vitamin B_{12} in megalocytic and macrocytic anemia; if full restitution is not attained, liver and/or stomach preparations can be given, perhaps with the addition of vitamin B_{12}.

BOOK REVIEWS

The Metabolic Response to Surgery. By Francis D. Moore, M.D., Moseley Professor of Surgery, Harvard Medical School, Boston, and Margaret R. Ball, A.B. Publication number 132, American Lecture Series, monograph in American Lectures in Surgery. Edited by Michael E. De Bakey, M.D., Professor of Surgery, Chairman of Department of Surgery, Baylor University College of Medicine, Houston, and R. Glen Spurling, M.D., Clinical Professor of Surgery, University of Louisville, Louisville, Ky. Cloth. $7.50. Pp. 156, with 48 metabolic diagrams by Mildred B. Codding, A.B., M.A., Surgical Artist, Department of Surgery, Harvard Medical School, Peter Bent Brigham Hospital, Boston. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 49 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto, 2B, 1952.

This book describes studies carried out on metabolic balances in order to determine the biologic responses to surgery. The studies deal with patients undergoing surgery who had been treated by ordinary methods. A uniform method of charting is presented, and, although an attempt has been made to present it simply, it has become cumbersome and confusing as can be noted in figure 31 on page 83. Charting of this type, although accurate and conclusive, must be simplified if it is to be of practical value, particularly to the general practitioner or the general surgeon.

Great detail was gone into in the preparation of this material, and the authors utilized a "team" of 35 co-workers. Careful studies were made on total intake and total output of selected chemical substances in order to cast light on biologic processes. The collection of output presented special problems. When dressings were stained by exudate or gastrointestinal contents, they were either soaked in distilled water or put through a small washing machine with distilled water, and this water was analyzed for nitrogen and electrolytes. Operative blood loss was measured calorimetrically, utilizing acid hematin on sponge rinsings; this was checked by total nitrogen.

This book is not easy to read. The need for profound study detracts from its practicability; however, it is a sincere study and may be of reference value as further studies dealing with these metabolic responses are carried out. The two most appealing sections are those dealing with facts and corollaries and surgical diet and parenteral supplements.

Child Psychiatric Techniques: Diagnostic and Therapeutic Approach to Normal and Abnormal Development through Patterned, Expressive, and Group Behavior. By Lauretta Bender, B.S., M.A., M.D., Professor of Clinical Psychiatry, New York University College of Medicine, New York. Cloth. $8.50. Pp. 335, with 55 illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 49 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto 2B, 1952.

The author of this volume is well known for her work on the psychology of perception and her "visual motor Gestalt" test, which is used extensively by psychologists. In this book Dr. Bender describes the technique she uses in treating psychiatric conditions of childhood. The work is based on the results obtained in the reexamination of thousands of problem children at the psychiatric division of the Bellevue Hospital. Some of these children were first examined when they were very young and were reexamined during adolescence. Parts of the book were published previously but are now unified. Some of the work was done with other authors, notably the late Paul Schilder.

The book will be of great value to psychiatrists, psychologists, and play therapists, but it will also be of interest to the general physician. Some chapters will be of special value to pediatricians, notably the ones on form as a principle in the play of children, the drawing of a man by children with chronic encephalitis, the art of high grade mental defective children, and group activities on a children's ward. Although the book is technical, the author's style is simple. The illustrations, many of which are freehand, add to the value of the book.

The reviews here published have been prepared by competent authorities and do not represent the opinions of any official bodies unless specifically stated.

American Universities and Colleges. Mary Irwin, Editor, American Council on Education. Sixth edition. Cloth. $10. Pp. 1105. American Council on Education, 1785 Massachusetts Ave., N.W., Washington 6, D. C., 1952.

American Junior Colleges. Edited by Jesse P. Bogue, Executive Secretary, American Association of Junior Colleges. Third edition. Cloth. $7.50. Pp. 604, American Council on Education, 1785 Massachusetts Ave., N.W., Washington 6, D. C., 1952.

"American Universities and Colleges" contains full descriptive data on 904 accredited universities and colleges in the United States, Alaska, Hawaii, and Puerto Rico. The new feature in this edition is the arrangement of institutions by states, with an institutional index instead of the former alphabetical listing by name only.

Part 1 of the book is devoted to professional education. Discussion on medical education by Dr. D. G. Anderson, Secretary of the American Medical Association Council on Medical Education and Hospitals, is concluded by a list of accredited medical schools. Dentistry, pharmacy, nursing, and veterinary medicine are adequately discussed.

The companion book, "American Junior Colleges," contains descriptions of 575 accredited junior colleges in the United States. This list is also arranged by states, with data on R. O. T. C. units and other features. These two publications are indispensable reference tools in any library, college, or office concerned with higher education.

The United States Public Health Service 1789-1950. By Ralph Chester Williams, M.D., Assistant Surgeon General, United States Public Health Service, Washington, D. C. Cloth. $7.50. Pp. 890, with illustrations. Commissioned Officers Association of United States Public Health Service, Box 5874, Bethesda, Md., 1951.

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This excellent history of the United States Public Health Service is well written, carefully documented, and impressive in its scope. The author is a regular career officer of the service, with broad experience in many different departments of the service. The presentation is effective, the typography good, and the photographic material of unusual historical interest.

The dramatic role of the Public Health Service in protecting the American people from communicable disease introduced from other countries is particularly well told. The innumerable other health activities, curative, educational and preventive, are also described at length in an interesting and stimulating fashion. The United States Public Health Service emerges from this history as a noble career service, dedicated to preserving the health of the people within the framework of the policies adopted by Congress and singularly free from the political storms that have afflicted many other federal agencies. If the author fails to note and record the occasional policy errors and internal dissensions that must have occurred some time in the long history of the United States Public Health Service, he may be forgiven, for the total story is true, an exciting, fruitful history of physicians devoted to public service in the finest tradition of medicine.

Atlas of Genito-Urinary Surgery. By Philip R. Roen, M.D., F.A.C.S., Instructor in Urology, New York Post-Graduate Medical School, New York. Introduction by Clarence G. Bandler. Cloth. $8. Pp. 325, with illustrations by Charles Stern. Appleton-Century-Crofts, Inc., 35 W. 32nd St., New York 1, 1951.

As indicated by the title, the author has compiled, with the aid of an excellent artist, a series of line drawings illustrating most of the common operations performed on the genitourinary system. The text, which describes each operation, is brief and direct, often being less than half a page in length, and is placed on the page opposite the illustration to which it refers. There is an illustration on every other page of the book. The book was planned for the resident, the young urologist, and the general surgeon who is occasionally required to perform a urologic operation. Only standard surgical procedures are discussed, although, in some cases, multiple procedures are illustrated for a given type of operation. Details of surgical technique are not

included, but the principles and successive steps of a given operation are outlined.

The book is divided into nine sections dealing respectively with general principles of urologic surgery, operations on the kidney, adrenal gland, ureter, bladder, prostate, scrotum and testicles, and urethra and penis. An index is included. The author draws from his experience in learning, teaching, and practicing urology for his discussion of the essentials of standard urologic operations that he has found useful and practical. The material is discussed in an easily understandable form, with clear illustrations and a minimum amount of text. The book is neither a textbook for the medical student nor a reference book, as no bibliographic references are included, and descriptions of many less common procedures are omitted, but it should be a useful manual for those not too familiar with urologic surgery. Although not everyone would agree with certain practices suggested by the author, such as the use of oxidized cellulose gauze imbedded in the renal parenchyma and the use of carbolic acid in surgical treatment of solitary renal cyst, his opinions, in general, coincide with current urologic practice. Indications for and relative evaluation of various surgical procedures are not included. The book is beautifully and completely illustrated and provides a quickly available source of information pertaining to urologic surgery.

Symposium über die Beeinflussung des reaktiven Geschehens durch Hypophyse und Nebenniereninde. Veranstaltet von der Schweizerischen Akademie der medizinischen Wissenschaften 30. September bis 2. Oktober 1951 in Zürich. [In German, English and French.] Sonderausgabe von Fasc. 1/2, Vol. 8 des Bulletin der schweizerischen Akademie der medizinischen Wissenschaften. Paper. 16 Swiss francs. Pp. 228, with 75 illustrations. Benno Schwabe & Co., Klosterberg 27, Basel 10; imported by Grune & Stratton, Inc., 381 Fourth Ave., New York 16, 1952.

This monograph consists of a series of 20 papers on the effects of cortisone and corticotropin (ACTH); they were read at a meeting of the Swiss Academy of Medicine at Zürich in September, 1951. The first 12 papers deal with tissue reactions, the next 2 with hemorrhagic states, and the last 7 with allergic reactions and their influence. They are written in English or German, depending on the nationality of the author, and there are brief discussions by participants at the symposium at the end of each paper. Almost all the material is based on the authors' own work, which by now has been published through the usual channels. Those interested in the experimental field will find this collection valuable, particularly the criticisms and comments of the discussants. Like similar collections that have appeared elsewhere, the work throws light on the fundamental mechanism of action of corticotropin and cortisone. The papers deal with such diverse topics as the effect of cortisone on trichophytosis in guinea pigs (Sonck and Miescher), the relation of the endocrine system to tissue reactions in tuberculosis (Rössler), the effect of cortisone on the tuberculin reaction (Ballabro and Sala), the Arthus phenomenon (Uehlinger), its site of action (Studer), and its relation to anaphylaxis (Dougherty). Of more clinical interest are papers dealing with corticotropin and cortisone therapy of asthma (Rose), ulcerative colitis (Weissbecker), and eczema (Miescher).

Today's Science and You. By Lynn Poole, Producer of Johns Hopkins TV Science Review. Cloth. $2.75. Pp. 208, with illustrations by Jeanne Bendick. McGraw-Hill Book Company, Inc., 330 W. 42nd St., New York 18; Aldwych House, Aldwych, London, W.C.2, 1952.

Many of the discussions in this small volume seem to offer little in the way of helpful education. This may be because the discussion does not relate the various scientific advances closely enough to what the average man knows. For example, it will not profit a man much to know that there is a device capable of seeing 100,000 colors, that the perfect fly repellent has yet to be developed, or that different shaped knobs on the automobile panel can simplify car operation. These and other scientific findings reported are interesting but open to so many arguments that their value may be questioned. Nevertheless, there is a considerable amount of interesting material. Anyone who has watched the Johns Hopkins Science Review on television will agree that many extremely stimulating programs have been presented. Perhaps the lesson from this is that science teaching can be effective only when it is given in the real-life pattern for which television is unique.

The Diagnosis and Treatment of Intrathoracic New Growths. By Maurice Davidson, M.A., D.M., B.Ch., Consulting Physician to Brompton Hospital for Consumption and Diseases of Chest, London. With chapter on Radiotherapy by David W. Smithers, M.D., M.R.C.P., D.M.R., Professor of Radiotherapy, University of London, and chapter on Operative Treatment by Oswald S. Tubbs, M.A., M.B., B.Chir., Thoracic Surgeon to St. Bartholomew's Hospital, London. Cloth. $8.75. Pp. 260, with 170 illustrations. Oxford University Press, 114 Fifth Ave., New York 11; Amen House, Warwick Sq., London, E.C.4, 1951.

As a rule, when a senior British physician produces a volume on a clinical subject, one can expect a clear, readable, and balanced presentation. This monograph is no exception. The author brings his extensive clinical experience to bear on a topic that is of immense practical importance today. The point of view is that of the general physician who, encountering tumors of the chest in his practice, is seeking reliable information in regard to the present methods of treating them. The material is discussed according to pathological entity. Each tumor or class of tumors is discussed according to its morbid anatomy, clinical diagnosis, and treatment. This is not, however, merely a handbook of differential diagnosis or a manual of diagnostic tests but a careful description of pathological processes supported by well-documented and pertinent clinical examples.

A large portion of the book is devoted to carcinoma of the bronchus. The discussion is that of the intelligent physician's point of view toward surgery of the lung. Surgical treatment is measured against radiation therapy and chemotherapy. The latter are discussed at length together with excellent practical advice for the treatment of the "untreatable" patient.

The chapter on mesoblastic growths provides an account of pleural endothelioma and related tumors. The confusing aspects of this problem are well illustrated by specific examples. Separate chapters on the techniques of radiation therapy, by Smithers, and standard thoracic surgical procedures, by Tubbs, complete the volume.

This book can be highly recommended as an intelligent correlation of fundamental pathology and wide clinical experience. It should be of great service both to the general practitioner and his expert consultant. It should provide excellent background material for medical students and residents and should find a place in any well-equipped hospital library. The text is delightfully written, and the illustrations are superb.

Fractures and Joint Injuries. Volume I. By Sir Reginald Watson-Jones, B.Sc., M.Ch.Orth., F.R.C.S., Orthopædic Surgeon to His Majesty the King, London. Fourth edition. Cloth. $22 per set. Pp. 443, with 709 illustrations. Williams & Wilkins Company, Mount Royal and Guilford Aves., Baltimore 2, 1952.

In every era of medicine, certain select treatises have profoundly influenced medical education and practice. Sir William Osler's "Textbook of Medicine" is an outstanding example. In the field of traumatic surgery, Sir Reginald Watson-Jones' "Fractures and Joint Injuries," the first volume of the fourth edition of which has recently been published, is another.

The first edition of this important textbook was published in 1940, at the beginning of the great conflict that was shortly to engulf mankind. It described clearly and concisely the principles underlying the treatment of fractures and joint injuries, and it can be said that, perhaps more than any other surgical text of our time, it became the "bible" of surgeons in every land, confronted as they were then by a host of complicated orthopedic injuries. It raised the standards of treatment incalculably, and untold thousands owe life, limb, and happiness to its author. Since 1940, successive editions have been published, each in its turn revised and rewritten to incorporate the experience gained by Sir Reginald in his unique vantage point as civilian consultant in orthopedic surgery to the Royal Air Force and more recently as director of the orthopedic and accident service at the London Hospital.

The fourth edition has been carefully revised to include recent advances in the treatment of fractures and joint injuries, and many new illustrations have been added. The physiology and pathology of bone repair are carefully and wisely discussed, and the all-pervading principles of treatment stressed. In chapter 6, there is a valuable discussion of vascular injuries, immersion foot, frostbite, and the crush syndrome. In the discussion of nerve injuries in chapter 7, the Seddon and Cohen classification

of nerve injuries is retained, but perhaps a more venturesome policy of earlier nerve exploration and repair would seem justified with the present advantages of chemotherapeutic control of infection. The section on clinical and radiographic diagnosis is of great value and should be read and reread by all practicing surgeons.

A wise and balanced conservatism governs the author's advice on the operative reduction of certain fractures, and, in the present volume, the great value of intramedullary nailing of certain fractures, notably of the femur, is commented on. The chapter on reactions of bone to metal is a most welcome addition to the present edition. It stresses that the use of plates, screws, and nails are merely methods of internal suture, which, in fact, introduce foreign bodies not unlike sequestra. This is an important observation that may well temper our present and perhaps premature advocacy of prosthesis in the treatment of avascular necrosis of the head of the femur and osteoarthritis of the hip joint.

A new and valuable addition is the chapter on shock, stress, and the adaptation syndrome, the invariable complications of all major injuries. The discussion and advice tendered is sound and practical. The section on open fractures and joint injuries has been greatly enhanced in value by important sections on the chemotherapeutic control of infection, the early closure of wounds by secondary suture or skin grafting, and the role of plastic surgery in fracture treatment. Few procedures are more important, and, until recently, more neglected. The last chapters of the book deal with fatigue and stress fractures, birth fractures, and pathological fractures. They are of immense value, and perhaps nowhere else has so much recondite information been so clearly assembled.

The plates and illustrations are excellent throughout, demonstrating clearly the author's discussion. The style is clear, straightforward, and to the point. The type is easily read and the paper used of excellent quality. In addition, the book is of manageable proportions. This book is a fine achievement, worthy of its distinguished author and of British surgery.

Lehrbuch der Röntgendiagnostik. 5. und 6. Lieferungen: Innere Organe. Von H. R. Schinz, W. E. Baensch, E. Friedl, und E. Uehlinger. Nebst Beiträgen von E. Brandenberger et al. Fifth edition. Paper. 84 marks; 98 marks. Pp. 1921-2356, with 522 illustrations; 2357-2884, with 507 illustrations. Georg Thieme, Diemershaldenstrasse 47, (14a) Stuttgart O; agents for U. S. A., Grune & Stratton, Inc., 381 Fourth Ave., New York 16, 1951; 1952.

For the review of sections 1 to 4 (*J. A. M. A.* **144:**885 [Nov. 4] 1950; **146:**1542 [Aug. 18] 1951) this reviewer had access to a privately owned copy of the fourth edition, but the edition available at his own institution and the one generally available in the United States is the third and, in the present review of sections 5 and 6, comparisons, of necessity, are between the third edition published in 1932 and this fifth edition published nearly 20 years later.

These two sections contain 962 richly illustrated pages dealing with the thorax in health and disease and will be followed by still more material on the cardiovascular system as a part of section 7. The space devoted to the normal thorax has been doubled and now includes a consideration of microfilming, a detailed description of the technique of bronchography with water soluble contrast media, and a consideration of normal lung architecture as seen in bronchograms.

The pages dealing with nontuberculous diseases of the trachea, bronchi, and lungs have been expanded from 91 in the third edition to 354 in the fifth. Particularly noteworthy are the passages on congenital anomalies of the bronchi and the appearance of the bronchial tree in various types of bronchitis. Aspirated foreign bodies, pulmonary neoplasm, and the various pneumonias are adequately discussed and illustrated, and in addition to the so-called dust diseases the authors include a description of the findings following aspiration of aqueous and nonaqueous fluids and the inhalation of gases. For the mycotic pulmonary diseases the authors have turned largely to the American literature. Lung cysts, lung abscesses, and parasitic diseases of the lung are discussed and well illustrated. The story of pulmonary tuberculosis, which was told in 72 pages in 1932, takes up 113 pages in the new edition. One hundred and eighty pages are devoted to diseases of the pleura, diaphragm, and mediastinum, and these are followed by 27 pages of tables and sketches summarizing the criteria for the differential diagnosis of pulmonary disease.

The final 215 pages of section 6 are given over to the roentgen findings in the normal and diseased heart, pericardium, and great vessels, and this same subject will be continued as part of section 7, which is to follow. In 1932, 116 pages were considered adequate for this subject, but radiology has made great strides in 20 years. Much of the added material is concerned with angiography, a subject that was barely mentioned in 1932.

It is hard to conceive of a textbook of radiology more complete or more dependable than this magnificent fifth edition, which reflects so well the enormous development that has occurred in clinical radiology within two decades. In 1932, three authors plus six collaborators sufficed, but today four authors and 13 collaborators are required. The authors remain authors, however, and not mere editors, so that one finds a completeness, unity, and minimum of repetition that is apt to be lacking in a compilation by a group of individually competent contributors.

Einführung in die Röntgenologie: Ein Lehrbuch für Ärzte und Studierende. Von G. F. Haenisch, a. o. Prof. Dr. med., Chefarzt i.R. am allgen. Krankenhaus Barmbeck, Hamburg, und H. Holthusen, o.ö. Prof. Dr. med., Chefarzt am allgemeinen Krankenhaus St. Georg, Hamburg. Mit einem physikalisch-technischen Beitrag. Von A. Liechti. Fifth edition by W. Fehr. Cloth. 60 marks. Pp. 521, with 371 illustrations. Georg Thieme, Diemershaldenstrasse 47, (14a) Stuttgart O; agents for U. S. A., Grune & Stratton, Inc., 381 Fourth Ave., New York 16, 1951.

The chief authors of this extensive introduction to roentgenology are well known to Americans. This edition is greatly expanded beyond the first edition of 1933. There are 44 pages devoted to physical and technical background, and the section on diagnosis, by Dr. Haenisch, is 240 pages long. The second half of the book, by Holthusen, is a masterly exposition of the field of roentgen and radium therapy. Radioactive isotopes are fully described, and growth disturbances following gamma irradiation are discussed and illustrated. This is an area that has been neglected in American literature. Delayed or late damage to the skin and internal organs receives extensive attention as does irradiation sickness. The field of superficial and deep therapy is covered with a staccato brevity and yet a thoroughness that is characteristic of Holthusen as Americans know him. For a textbook on an introduction to roentgenology, Haenisch does not seem to have spared an area of useful exposition and illustration. One cannot escape the recollection of the story of the German who, in a prize competition on the elephant, offered three volumes entitled, an introduction to the study of the elephant. The authors have compressed their contribution into one volume, apparently without missing any single important segment of roentgenology. The quality of paper, the contrast in the lithographs, and the quality of the printing surpass the average, comparable, American textbook.

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Contractor's Final Report on Artificial Arm and Leg Research and Development Covering the Period January 2, 1945, to December 31, 1950. Submitted by Northrop Aircraft, Inc. Contract number VAM-23062. National Research Council Committee on Artificial Limbs Advisory to Veterans Administration and the Office, Surgeon General, United States Army. This report compiled and written by Gilbert M. Motis. Cloth. Pp. 358, with illustrations. Northrop Aircraft, Inc., Northrop Field, Hawthorne, Calif., 1951.

This report is a detailed technical description of the application of modern engineering principles and materials to the problems of increasing the functional efficiency of the prosthesis and its attachment to the amputee. The design of many devices by Northrop engineers was facilitated by basic data derived from time and motion studies of arm and leg improvement made by the University of California at Los Angeles and the University of California (Berkeley). This work will serve as a valuable reference book to those concerned with the manufacture and fitting of prosthetic units and will be a stimulus for further research.

There is an interesting chapter on x-ray cinefluorographic technique and a short appendix on an experimental infant prosthesis. Northrop has produced a good upper extremity prosthesis that satisfies all basic maker's requirements and standard prerequisites of light weight, durability, comfort, and ease of operation. There are numerous detailed drawings and photo-

graphs of the prosthetic units, their component parts, and of the attachment of these units to the amputee. This represents a distinct advance in the mechanism of artificial limbs, and the book may be read with interest by those who are interested in the problems of amputees.

Clinical Applications of Recreational Therapy. By John Eisele Davis, Sc.D., Chief, Corrective Therapy, Veterans Administration, Washington, D. C. Publication number 123, American Lecture Series, monograph in American Lectures in Physical Medicine. Edited by W. A. Selle, Ph.D., Professor of Biophysics, University of California Medical School, Los Angeles. Cloth. $3.75. Pp. 118, with 21 illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 49 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto 2B, 1952.

The author of this monograph attempts to supply a basic philosophy for the employment of "free play, exercise, and activity" in rehabilitation, especially from the viewpoint of psychodynamics. The 44 sections are distinct essays that usually take some previous publication as a text. Such topics as the psychological appeal of free play and recreational techniques based on concepts of milieu therapy are discussed.

This book is mainly concerned with the rehabilitation of patients institutionalized for psychiatric purposes. The number of these patients is increasing. The effects of institutional life on their initiative can be deadly, and many are not interested in doing anything that would be useful to others or to themselves. Even so, some readers will feel that this book unduly emphasizes recreational as distinguished from occupational therapy. The meticulous, expensive forms of recreational therapy suggested need not only be rationalized on the basis of theory but must also be defended on the basis of more practical considerations. With respect to the latter, the book leaves something to be desired. It must, however, be commended, as it is well written and attractively illustrated.

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Fertility in Men and Women: The How and Why of Having Children. By James Alan Rosen, M.D., Attending Obstetrician and Gynecologist, Lincoln Hospital, New York. Edited with introduction for Health Series by Harry Swartz, M.D. Cloth. $3. Pp. 177. Coward-McCann, Inc., 210 Madison Ave., New York, 1952.

This little book is the first of a projected health series, under the general editorship of Dr. Harry Swartz. This volume is prepared for the lay reader, particularly those couples who have infertility problems. The author discusses the anatomy and physiology of the male and female reproductive apparatus and the techniques and methods used in diagnosing the contributory defects. There are chapters on treatment to alleviate the complaint and an attempt at evaluation of artificial insemination as a mode of treatment in infertility problems. The information offered is technically sound and should be clear to the lay reader, but the chapters lack the style and clarity of other recent books offered to the laity. The author includes a chapter of typical case histories, which might have some usefulness but suffer from lack of professional detachment and objectivity. The format of the book is attractive. The two illustrations are crudely designed. A useful glossary of technical terms is appended.

Handbook of Basic Microtechnique. By Peter Gray, Ph.D., D.I.C., Head, Department of Biological Sciences, University of Pittsburgh, Pittsburgh. Cloth. $3. Pp. 141, with 57 illustrations. Blakiston Company (Division of Doubleday & Company, Inc), 1012 Walnut St., Philadelphia 5, 1952.

This is intended as a useful handbook for the student or technician faced with the problem of preparing animal or plant material for microscopic examination, and supplements Gray's "Handbook of Basic Microtechnique," a larger reference work now in preparation. It is an inexpensive book for quick consultation on microtechnical procedures. Part 1, devoted to materials and processes of slide making, has chapters on materials and equipment, fixation and fixatives, stains and staining, dehydrating and cleaning, mounts and mountants, making whole mounts, making smears, making sections, and cleaning, labeling, and storing slides. Part 2, devoted to specific examples of slide making, has 15 short chapters on the preparation of whole mounts, bacterial stains, and certain histological sections. This handbook meets its objectives in full and is recommended to students or technicians engaged in histological procedures.

Symposium on Geographical Pathology and Demography of Cancer. Council for Coordination of International Congresses of Medical Sciences under auspices of World Health Organization and United Nations Educational, Scientific and Cultural Organization, session held at Regent's Park College, Oxford, England, July 29 to August 5, 1950. Chairman: Prof. J. H. Maisin. Editor: Dr. J. Clemmesen. Cloth. Pp. 152, with illustrations. The Council, 19, Ave., Kléber, Paris 16e, [n.d.].

This volume contains the papers read at a symposium held in Oxford, England, in 1950, under the chairmanship of Prof. J. H. Maisin and sponsored by the World Health Organization (WHO) and the United Nations Educational, Scientific, and Cultural Organization (UNESCO). Several papers are devoted to statistical variations in cancer incidence between different countries or within a single country. A paper by R. Doll on the etiology of cancer of the lung, especially the correlation between incidence among tobacco smokers and nonsmokers is a careful statement of current English studies. Other papers analyze cancer incidence in India, Indonesia, and North Africa in relation to nutrition and food habits, environment, and other disease states. Dr. Symeonidis from the National Cancer Institute introduces interesting observations on the relationship of poststarvation gynecomastia in Greece to hormonal imbalance and its implication as a factor in breast cancer. The administrative aspects of geographic pathology as now being developed at the National Cancer Institute are described by H. L. Stewart. Cancer demography is emerging as a definite field, and the contributors to this symposium have indicated the scope and range of investigations now developing in this field in a most effective manner. Discussions by members of the conference are included for each chapter. Each paper has an abstract in both French and English. The volume is well printed, and the graphs and charts are clear and legible. The microphotographs are poor.

Elsevier's Encyclopædia of Organic Chemistry. Founded by E. Josephy and F. Radt. Edited by F. Radt. Series III, Carboisocyclic Condensed Compounds. Volume 14, Supplement: Tetracyclic and Higher-Cyclic Compounds Except Steroids and Triterpenes. [Cumulative index]. Cloth. $88; $77 to subscribers to series III; $66 to subscribers to complete work. Pp. 938 S; 113. Elsevier Press, Inc., 402 Lovett Blvd., Houston 6, Texas; 118 Spuistraat, Amsterdam, Netherlands, 1951.

Volume 14 in the regular series of this work covered the literature on tetracyclic and higher cyclic compounds up to and including 1936. The growth of studies on these compounds has been so rapid since that time that the editors have published a supplement that brings the literature up to 1946. The amount of work done on these substances in that 10 year period has increased to the extent that it is necessary to publish the supplement in two volumes. The first of these two volumes is now available and covers all tetra and higher cyclic compounds with the exception of the steroids and triterpenes, which will appear in the second volume.

The subject index includes references to both the main volume and the supplement, with a compilation of all substances that fall into this chemical class under such index headings as carcinogenic compounds, estrogenic compounds, and naturally occurring compounds in coal tar, minerals, and plants. Such features as a summary table of the carcinogenic activities of 1,2-benzanthracene derivatives is included. The physiological properties of many interesting parent compounds and their more important derivatives are discussed. Among those discussed in the present supplement are fluoranthene, naphthacene, benzanthracene, dimethyl-benzanthracene, chrysene, benzophenanthrene, pyrene, dibenzofluorene, cholanthrene, 20-methyl-cholanthrene, dibenzanthracene, benzopyrene, and hypericin.

Contractura isquémica de Volkmann. Por F. Bastos Mora. Cloth. Pp. 119, with 44 illustrations. Publicaciones médicas José Janés, editor, Muntaner 316, Barcelona, 1951.

This is a detailed, well-written monograph that covers the subject thoroughly. The author has evidently drawn from extensive experience with this condition. The pathogenesis and pathology of Volkmann's contracture are discussed in detail. The complete clinical picture from the time of initial injury to the final tendon transplant is discussed clearly, concisely, and adequately. Alternative methods of surgical reconstruction are also discussed. The illustrations are satisfactory and the bibliography good. This work will prove exceedingly useful to those interested in Volkmann's contracture.

QUERIES AND MINOR NOTES

ALLERGY AND DUODENAL ULCER

TO THE EDITOR:—*Is allergy still recognized as a cause of duodenal ulcer? Can food allergy aggravate an existing duodenal ulcer?* *M.D., Ohio.*

ANSWER.—A discussion of allergic factors in the pathogenesis of duodenal ulcer by Andresen and Grossman may be found in the book entitled "Peptic Ulcer" (edited by Sandweiss, D., Philadelphia, W. B. Saunders Company, 1951). It is clear, as the result of a wide variety of experimental studies, that allergic reactions can be produced in the mucous membrane of the stomach or the duodenum very much as they can be produced in the skin. For the most part, however, they heal readily and do not give rise to chronic, progressive ulcers resembling those seen in man or those produced in experimental animals either by the Mann-Williamson procedure or by the transplantation of the antrum of the stomach into the colon by the method of L. R. Dragstedt and his associates. Andresen believes that an allergic response to some of the products arising in the body as a result of foci of infection may produce typical ulcers and may also cause their recurrence. He suggests that the beneficial effects of removal of foci of infection may in part be due to these factors. Most of the experimental and clinical evidence at present available indicates that duodenal and gastrojejunal ulcers are due to the corrosive properties of the gastric content that are greater than normal because of hypersecretion of gastric juice in the fasting stomach as well as after the ingestion of food. This hypersecretion is thought by Dragstedt to be of nervous origin, and this is the basis for the vagotomy operation.

CEPHALIN FLOCCULATION TEST IN HEPATITIS

TO THE EDITOR:—*Is information available on the length of time a cephalin flocculation test remains positive after a patient is clinically free from hepatitis?*

F. A. Nause, M.D., Sheboygan, Wis.

ANSWER.—It is difficult to give a categorical answer to this question without knowing the technique of the cephalin cholesterol flocculation test performed. As a general rule, the test becomes negative at or about the time the serum bilirubin returns to a normal figure. This was the general experience with volunteers and has been confirmed many times in studies on the naturally occurring form of the disease. In a recent study from the army hepatitis center in Germany, only 10% of 667 patients studied had a positive cephalin cholesterol flocculation test by the end of the fourth week of the disease when the 48-hour flocculation test was used. When the 24-hour flocculation test was used, the percentage of positive tests at the end of the fourth week was more than twice as high. By the end of the third month of the disease, only about 2% of the 48-hour flocculation tests were still positive (Neefe, J. R.; Gambescia, J. M.; Gardner, H. T., and Knowlton, M.: Comparison of the Thymol, Cephalin-Cholesterol Flocculation and Colloidal Red Tests in Acute Viral Hepatitis, *Am. J. Med.* **8**:601 [May] 1950).

Sborov and Keller have recently presented figures on patients with the mildest form of the disease: 74% of patients with serum bilirubins of less than 5 mg. per 100 cc. had negative cephalin flocculation tests by the third week of the disease. In patients who had serum bilirubins at a higher level a much higher incidence of positive tests was obtained. In general, one may say that a patient who has a positive cephalin cholesterol flocculation test, which persists beyond the third month from the onset of jaundice, deserves investigation by other methods to be certain that subacute or chronic hepatitis is not developing.

The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any official bodies unless specifically stated in the reply. Anonymous communications and queries on postal cards cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

LUMBAR MENINGOMYELOCELE

TO THE EDITOR:—*I repaired a lumbar meningomyelocele on a 1-day-old infant. The surgical procedure was uneventful, and the child has done reasonably well. Two weeks later, a neurosurgeon who examined the child said the repair should not have been done, because it was unnecessary and the removal of a sac from which fluid might be absorbed would cause hydrocephalus. We have had, in our hospital, about six of these infants in the last two years. None of them were treated surgically, and hydrocephalus developed in all of them. It is difficult for me to understand how absorption of fluid from the spinal canal (arachnoid) could, in any way, affect an internal hydrocephalus and why repair of a meningomyelocele would have anything to do with the development of hydrocephalus. What is the proper treatment of a lumbar meningomyelocele without skin covering?* *M.D., Texas.*

ANSWER.—The selection of patients with lumbar meningomyelocele who can be surgically treated must of necessity be on an individual basis. The surgeon should elect to operate only on those patients whom he believes he can help. The fact that it is surgically possible to repair the defect on the back is not, in itself, sufficient indication for operation. Children whose legs are paralyzed, who have a loss of sensation in the sacral distribution, who have a paralysis of bowel and bladder, or in whom a hydrocephalus is developing, are not suitable candidates for surgical repair of the deformity.

There is no good evidence that removal of the meningocele sac is responsible for the development of hydrocephalus. On the contrary, the study of a large number of cases has shown that hydrocephalus develops as frequently if the meningocele is not operated on. This is not surprising, because pathological studies demonstrate that the abnormality responsible for the hydrocephalus lies in the head and not in the spinal canal. It is true that the idea that the sac absorbs cerebrospinal fluid has been advanced, but it has not been generally accepted nor is it in accord with the facts.

If a congenital deformity of this nature is suitable for surgical repair, the redundant skin and meninges should be excised, the dura mater should be closed tightly, and fascial flaps should be reflected from the paravertebral muscles on both sides and imbricated over the defect in the spinal canal. The skin is then closed. No attempt should be made to close the bony defect.

LIVER BIOPSY

TO THE EDITOR:—*Please tell me the technique used for obtaining a needle biopsy specimen of the liver.*

J. C. Eakle, M.D., Sutton, W. Va.

ANSWER.—Liver biopsy can be performed to advantage with the "vim"-Silverman needle, a 14-gage needle having a hypodermic bevel tip. It contains an inner needle that is split longitudinally and has a cutting edge. After preparation of the skin and a preliminary dose of morphine sulfate, a small nick is made in the skin, usually at the right midclavicular line, just below the costal margin. The outer needle is inserted with the inner needle withdrawn, so that its point is above the bevel of the outer needle. The inner needle is then moved forward into the substance of the liver.

As it advances, it cuts out a small cylinder of liver tissue, about 2 mm. in width. The outer needle is then advanced over the inner needle, thus trapping the specimen, closing the prongs of the inner needle, and separating the innermost portion of the tissue to be removed. Both needles are then withdrawn simultaneously. The small specimen of tissue obtained, usually measuring 2 cm. by 2 mm., is, as a rule, adequate for a study of liver histology.

Most operators confine their biopsies to patients who have hepatomegaly and in whom the subcostal approach is possible;

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however, many who are more experienced do not hesitate to obtain specimens through the ninth intercostal space in the posterior axillary line. The risk of the procedure is relatively small, provided one avoids the danger of bleeding. Bleeding, coagulation, and prothrombin times should be determined routinely on all patients for whom liver biopsy is contemplated. If there is any evidence of there being an inflammatory process within the abdomen or at the right lung base, the procedure is contraindicated. About 5% of patients have some pain postoperatively; this usually disappears within a few hours. There is an excellent account of the various instruments and techniques used in an article by Hoffbauer (*J. A. M. A.* **134:**666 [June 21] 1947).

MILD CONVULSIVE SEIZURES IN INFANT

To the Editor:—*A primipara delivered a child easily following an uneventful pregnancy. An episiotomy was performed, but forceps were not used. The child at birth weighed 9 lb., 12 oz. (4,422.52 gm.) and seemed to be normal. About two and one-half months after birth, mild convulsive seizures developed in the child. During bottle-feeding or when he is lying at ease in the crib, he suddenly has clonic contractions of the arms and legs, with inconstant horizontal nystagmus. The first attack lasted about 30 seconds; subsequent ones have been less severe. After the first two attacks he cried loudly and long and then quieted down and was apparently normal. During the seizures he turns pale and appears to lose consciousness to varying degrees. During the first two attacks, the baby seemed to have colic. Recently, he has had a mild upper respiratory tract infection and had the last few attacks with the onset of the infection. The child has been examined by several pediatricians, all of whom gave the opinion that he is normal. An electroencephalogram was made by a neurologist, who reported normal results. The child eats well. I would appreciate a discussion of the etiology, treatment, and prognosis of this condition.*

Edgar E. Struve, M.D., Fullerton, Calif.

Answer.—With the normal birth history and normal results of physical examination, it seems reasonable to rule out birth injury as a cause for these attacks. Infantile tetany could be excluded as a cause by the rarity of its occurrence before the age of three months and by the lack of a history of rickets or of an abnormal condition observed during physical examination. The existence of a normal blood calcium level would eliminate the possibility of infantile tetany, as would normal reactions to electric stimulation. Parathyroid tetany is a rare condition caused by hypofunction of the parathyroid. When noted in infancy, it occurs in the period immediately after birth and is characterized by a low blood serum calcium level. Tetany may also be associated with alkalosis caused by vomiting and loss of acid gastric secretions, by hyperventilation, by the administration of salts that form insoluble calcium compounds, and by nephritis with chronic renal insufficiency, in which the level of inorganic phosphates of the blood serum rises and the level of blood serum calcium falls. In the case in question it is assumed that the results of urinalysis are normal and that no nephritis is present. These conditions include most of those that have a physical etiological basis and, from the data furnished, can probably be quite easily excluded from possibility.

Some functional conditions may give rise to the symptoms shown by this infant. Occasionally, an infant shows unusual susceptibility to many kinds of stimuli, and has prolonged spells of crying and muscle spasms causing flexion of the arms and legs and clenching of the hands. He is easily startled, frequently thrashes about, and may evidence breath holding and pallor; such a baby is termed a hypertonic infant. In the past, these babies were thought to suffer from vagotonia and were often treated with atropine. The exact pathogenesis of this condition is not clear, although heredity probably is an important factor. These infants respond favorably to hospitalization or the substitution for their care of a calm nurse for easily agitated parents. Mild sedation with phenobarbital sodium for several weeks is often helpful. The prognosis is generally good: the symptoms usually subside completely, and permanent emotional instability is not a necessary aftermath of this condition.

HYDROCEPHALUS AND SPINA BIFIDA

To the Editor:—*A child, who had mild hydrocephalus and severe spina bifida but was apparently normal otherwise, weighing 6 lb. and 15 oz. (3.15 kg.), died five days after birth. This was the mother's third pregnancy and her first son. Two other children are normal. The mother is one of three children, all girls, the first of whom had a congenital defect of the spine, described by the grandparents as typical of mild spina bifida. The mother also had two half-sisters, neither of whom had any congenital defects. There is no history of congenital defects in her husband's family. Are hydrocephalus and spina bifida definitely hereditary? If so, what were the chances of this child being affected, since two others were normal? What are the chances of a fourth or fifth child being normal? Could the mother's health during the third pregnancy have influenced the appearance of the defects? (She suffered from hypothyroidism, fairly well controlled by thyroid extract, 4 grains [0.25 gm.] daily, mild hypoglycemia, and moderately severe secondary anemia.) Does the sex of the child influence the likelihood of congenital defects of this type?*

M.D., Georgia.

Answer.—Ordinarily, neither hydrocephalus nor spina bifida is definitely hereditary. Spina bifida, with visible deformity on the back, such as a meningocele or a meningomyelocele, occurs in about one out of every thousand births. Spina bifida occulta, which is usually asymptomatic and often without external manifestation, occurs in about 5% of the population. This is in addition to spina bifida of the lowest sacral segments, which occurs in practically everyone. Occasionally, instances of congenital defects in the spinal column, associated with deformities of the nervous system, have shown a definite hereditary or familial tendency. In the present instance, the history, as given, is not sufficiently detailed to permit one to judge whether there is a familial tendency present here. The nature of the congenital defect said to have been present is not stated nor are we certain of the presence of congenital defects in some members of this family. In view of the inadequate information on these points, positive statements beyond those given above are not possible. The cause of the congenital deformities of the spine in persons in which they appear is unknown. It is conceivable that the mother's health could be a factor. Whatever the cause, it must be effective within the first month of intrauterine life. After that date, the development of the nervous system has proceeded to such a point that this type of deformity would not be possible. There is little evidence that sex of the child influences this type of congenital deformity. The matter is fully discussed in P. C. Bucy's "Spina Bifida and Associated Malformations" (in Practice of Pediatrics, edited by J. Brennemann, Hagerstown, Md., W. F. Prior Company, Inc., 1937, vol. 4, chap. 15.)

TREATMENT OF PAIN IN ARTHRITIS

To the Editor:—*Two products in tablet form have come to my attention for the treatment of rheumatoid arthritis. One contains p-aminobenzoic acid and the other, sodium gentisate. I am interested in knowing which drug has proven more effective in alleviating the pain of rheumatoid arthritis.*

Francis M. Walker, M.D., Rochester, N. Y.

Answer.—Sodium gentisate was reported in 1948 to be as effective as salicylates in relieving articular pain in rheumatoid arthritis; however, it possesses no special advantages over salicylate preparations, except that it may be tolerated in a patient who is unable to take either aspirin or sodium salicylate. *p*-Aminobenzoic acid, in common with other benzoates, exerts some analgesic action, although inferior to that gained from salicylates. About five years ago, its use in conjunction with sodium salicylate was studied. The conclusion was drawn that the blood salicylate level was thus increased, chiefly by means of decreasing the excretion of free salicylate. Determinations made subsequently have failed to confirm these findings, although a clinical study has shown that an enhanced analgesic effect may be obtained by the addition of *p*-aminobenzoic acid to oral doses of sodium salicylate. In the experience of many who treat rheumatoid arthritis, aspirin is more consistently effective than sodium salicylate in

relieving pain and stiffness and is therefore the drug chosen. Sodium salicylate may be substituted for patients who show gastric intolerance to aspirin in any form.

EFFECTS OF DIAGNOSTIC RADIATION

To the Editor:—*In several cases of apparently highly radiosensitive tumors, after routine initial diagnostic roentgenologic work-up (chest x-ray examination, gastrointestinal series, or urological radiographs), the hematological picture has shown an increase in hemoglobin, red blood cells, and thrombocytes, without any medication or change in food intake. Can it be that in the initial phase of the disease, the small dose of roentgen radiation thus incurred and directed unknowingly at the suspected cancer was effective in causing secondary hematopoiesis by inhibiting growth of the mass and metastases or in stimulating primary hematopoiesis?*

C. D. J. Generales, M.D., New York.

Answer.—It is likely that the amount of radiation received in certain diagnostic procedures can produce recession of highly sensitive malignant tumors, but it does not seem possible that the blood changes described could be due to a primary or direct effect on the hematopoietic system. The cells of the hematopoietic system are highly sensitive to radiation, but the effect of the latter is to produce destructive, rather than productive, changes. Neither does it seem probable that a destructive effect on a primary tumor or its metastases could produce the stimulative effect described. It seems more likely that the improved blood picture in the observed cases is either coincidental or due to improvement in the patient's general health.

ESTROGENS AND CANCER OF THE UTERUS

To the Editor:—*A 49-year-old patient with adenocarcinoma of the uterus and metastasis was elsewhere put on estrogen because of nervousness and other symptoms following bilateral ovariectomy. I am treating her with deep x-ray therapy, but I am not following the doctor's instructions about giving her estrogen, as I am a little skeptical, regardless of her menopausal symptoms. Is there definite proof that the administration of estrogen under these circumstances is a hazard?*

M.D., Alabama.

Answer.—There is no definite evidence that estrogens are carcinogenic. In spite of this inconclusive evidence, it is the opinion of a number of gynecologists that it would be better to withhold the hormone in patients who have carcinoma or who have had it. Cancer of the endometrium is not found frequently in the castrate, and Dockerty reports that prolonged, unopposed estrogen stimulation may be a factor in the production of such endometrial changes. Therefore, the usual menopausal symptoms in a woman of this age would best be controlled either with sedation or with the male hormone, testosterone.

PHARMACOLOGY OF MAGNESIUM SULFATE

To the Editor:—*Please summarize the pharmacodynamics of magnesium sulfate as related to its use in the treatment of toxemias of pregnancy. What, if any, are its toxic effects on the body? In three instances we observed gross hematuria after intramuscular injection of 10 to 20 cc. of 50% magnesium sulfate, and we are reasonably sure that bleeding did not occur from an indwelling catheter present at the time. Is it possible for a chemical nephritis to have occurred?*

W. R. Fallon, M.D., Chicago.

Answer.—Magnesium sulfate is used in the treatment of preeclampsia and eclampsia because of its sedative and vasodilator effects. These pharmacologic actions favor a decrease in the blood pressure and allay the convulsive seizures. The efficacy of the drug as a central nervous system depressant and as a vasodilator has been substantiated by experimental as well as clinical evidence. It is considered the most efficient drug for allaying the convulsions of tetanus. It has been used extensively in the treatment of hypertension and uremia because of its vasodilating effects. Haury has shown that the intravenous injection of magnesium sulfate produced marked dilatation of the splanchnic organs and the kidneys.

Magnesium sulfate is a respiratory depressant, and, when used in any dosage, it is prudent to have an antidote readily available in the form of a 10% solution of calcium chloride or calcium gluconate. Calcium salts should be administered slowly if the patient has been digitalized. Hematuria following the administration of magnesium sulfate has not been reported. The amount administered to this patient is not excessive, for as much as 35 gm. has been given to a patient during the first 24 hours of eclampsia without undue effects.

THE SCLERA IN CAROTENOSIS

To the Editor:—*Can hypercarotenemia produce yellowish pigmentation of the sclera as well as of the skin? If so, which appears first and why? Is there any relationship to jaundice?*

Max S. Lake, M.D., Salina, Kan.

Answer.—The yellow pigmentation of the skin known as xanthosis, or carotenosis, is caused by an excess of carotene in the blood and is most marked in the palms, soles, and nasolabial folds. In contrast to jaundice, the scleras usually remain clear. The differential diagnosis of xanthosis and jaundice depends on the history and other findings, a knowledge of the patient's diet, the concentration of bilirubin in the serum, the icterus index and the lipochrome index. When with yellow pigmentation of the skin a low value for the serum bilirubin and a high icterus index are present, the condition must be xanthosis; if the value for the serum bilirubin is high and the lipochrome index is low, the abnormal coloration is due to jaundice. If both the concentration of serum bilirubin and the lipochrome index are elevated, xanthosis and jaundice are associated.

REFERENCE:

Boeck, W. C., and Yater, W. M.: Xanthemia and Xanthosis (Carotinemia): A Clinical Study, J. Lab. & Clin. Med. 14:1129-1143 (Sept.) 1929.

TREATMENT OF SMALL AREA OF DRY GANGRENE ON ARM

To the Editor:—*Advice is requested regarding the treatment of an area of dry gangrene. The area is situated on the volar, medial aspect of the left upper forearm and is about 1 in. (2.54 cm.) by 1½ in. (3.81 cm.) in size. This condition developed after the paravenous injection of a small amount of 10% calcium levulinate. The black, dry, necrotic crust is sharply demarcated from the unaffected skin, which does not show any inflammatory reaction. On palpation, the underlying tissues and possibly the muscle appear to be affected by the necrotic wedge. There is no pain, but use of the left forearm is somewhat impaired.*

M.D., South Dakota.

Answer.—This necrotic lesion should be treated conservatively. In most instances, the necrotic area will slough off, and healing will take place spontaneously. If, after several months, this does not occur, surgical excision may be necessary, and granulation will then probably fill in the defect.

ACTIVITY AFTER OPERATION FOR UTERINE PROLAPSE

To the Editor:—*After a plastic operation for complete prolapse of the uterus, how soon can the patient be out of bed? How soon can she do heavy work, and how soon can she have sexual intercourse?*

M.D., Central America.

Answer.—The pattern of postoperative care has changed markedly in recent years. There is no reason why the patient cannot be allowed out of bed to the bathroom or to use a bedside commode the day after surgery. Early ambulation is desirable, because many of the patients are elderly and early activity decreases the hazards of thrombosis and infarction. Ambulation should be restricted during the first week. Heavy work should be postponed for at least eight weeks. Sexual intercourse is permissible six or eight weeks after surgery if the healing has been satisfactory. The administration of an estrogen, such as 0.5 mg. of diethylstilbestrol, each night for three or four months after surgery favors healing and the restoration of a normal vagina in the woman in the postmenopausal period.

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